

# RADIOLOGY

A MONTHLY JOURNAL DEVOTED TO CLINICAL RADIOLOGY AND ALLIED SCIENCES

Vol. 73

SEPTEMBER 1959

No. 3

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# RADIOLOGY

A MONTHLY PUBLICATION DEVOTED TO CLINICAL RADIOLOGY AND ALLIED SCIENCES  
PUBLISHED BY THE RADIOLOGICAL SOCIETY OF NORTH AMERICA

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## The Visualization of Internal Organs by Accentuation Scintillation Scanning Technics<sup>1</sup>

WILLIAM J. MacINTYRE, Ph.D., HYMER L. FRIEDEL, M.D., GODOFREDO GOMEZ CRESPO, M.D., and  
ABBAS M. REJALI, M.D.

IT HAS BEEN LONG recognized that radiation arising from selectively deposited radioelements may be used to record the spatial distribution of these elements so as to reflect the configuration and position of an organ structure. Although it had been shown previously that some concept of the general deposition of radioelements in the body could be established by making static counts of the accumulated radioactivity along a grid system, the later development of the automatic scintillation scanner (1, 2, 6) demonstrated the possibilities of graphic illustration of radioisotope distribution.

In its original concept, the automatic scanner was designed to delineate the regions of the thyroid gland or of thyroid-functioning sites by virtue of the avidity of thyroid tissue for radioactive iodine. Thus the problem was concerned mainly with delineating structures in which a steep differential in radioactivity existed between the region in question and its environment. In the application of scanning systems to the visualization of large organs, however, several problems arose which were not encountered in the original thyroid-scanning procedures.

Since the delineation of any specific organ is dependent upon obtaining a

differential uptake of some radioisotope, scanning technics have in general been concerned with maximizing this differential. In the problem of visualization of the thyroid gland by administration of  $I^{131}$ , for example, a greater differential may be obtained simply by increasing the dose of radioiodine. When, however, two sites are to be demarcated by some variation in structure (such as difference in vascularity), the differential is inherent in the anatomical configuration alone and cannot be made greater by administration of larger amounts of radioactive material. Similarly, the finding of a defect or absence of radioactivity which is surrounded by tissue with normal uptake is dependent entirely upon the ratio of the normal tissue to the abnormal tissue as subtended by the detector.

Wherever visualization depends upon the differentiation of minor variations in the uptake of the radioactive material, we have been primarily concerned with technics that would make readily perceptible small differences in the counting rates of the scanned area.

### TECHNICS

Two systems have been devised to accentuate small differences between the

<sup>1</sup>From the Department of Radiology, School of Medicine, Western Reserve University, Cleveland, Ohio. This work was performed primarily under A.E.C. Contract No. W31-109-eng-78, with Western Reserve University. Presented, as part of a Symposium on The Use of Isotopes in Diagnosis, at the Forty-fourth Annual Meeting of the Radiological Society of North America, Chicago, Ill., Nov. 16-21, 1958.

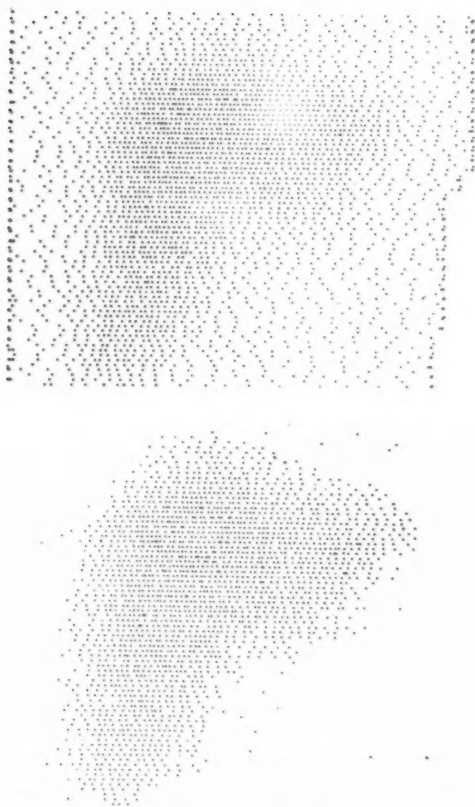


Fig. 1. Normal liver recorded with and without counting rate cut-off circuit following administration of 250  $\mu$ c of colloidal gold ( $\text{Au}^{198}$ ).

radioisotope uptakes of adjacent areas of a scanned region. The first has involved the introduction of a counting rate controlled cut-off circuit that permits the operator to select arbitrarily a counting rate below which no points are recorded. Any radiation reaching the counter above this predetermined level is recorded at its actual counting rate, while radiation reaching the counter below this level is completely eliminated. Small variations may now assume an infinite ratio of contrast with the surrounding environment, since counting rates below the selected level are not recorded. A normal liver is shown in Figure 1 as recorded with and without the counting rate cut-off circuit. Figure 2 shows a liver of similar configuration but containing a



Fig. 2. Hepatoscan illustrating a region of non-functioning liver tissue isolated in the left lobe. The patient had received 200  $\mu$ c of rose bengal ( $\text{I}^{131}$ ). (From Friedell, H. L., MacIntyre, W. J., and Rejali, A. M.: *Am. J. Roentgenol.* 77: 455, 1957.)

space-occupying lesion of non-functioning liver tissue (3). While the effect of the counting rate cut-off circuit is to give a clearer outline to the liver itself, this is not the only reason for its use. The primary purpose is to accentuate such an area as is illustrated in the left lobe of the liver (Fig. 2), which exhibits an atypical uptake of radioactive material. Thus, in this instance, where the drop in counting rate over this region was only 32 per cent, the actual visualization has greatly enhanced the decrease.

In respect to diagnosis, the scan itself can only indicate regions of greater or lower deposition of the radioactive material; in this case biopsy proved that the decrease was due to metastasis to the liver from a lung adenocarcinoma.

In the above technic, accentuation of the site under scrutiny has been accomplished by the complete elimination of low-activity areas rather than by increasing the response from the higher levels. For this latter effect, our second system has utilized a light-recording device for accentuating small differences in the counting rate (5). A simple method of synchronizing a light beam with the position of the detector head has been accomplished by coupling electromechanically the position of the

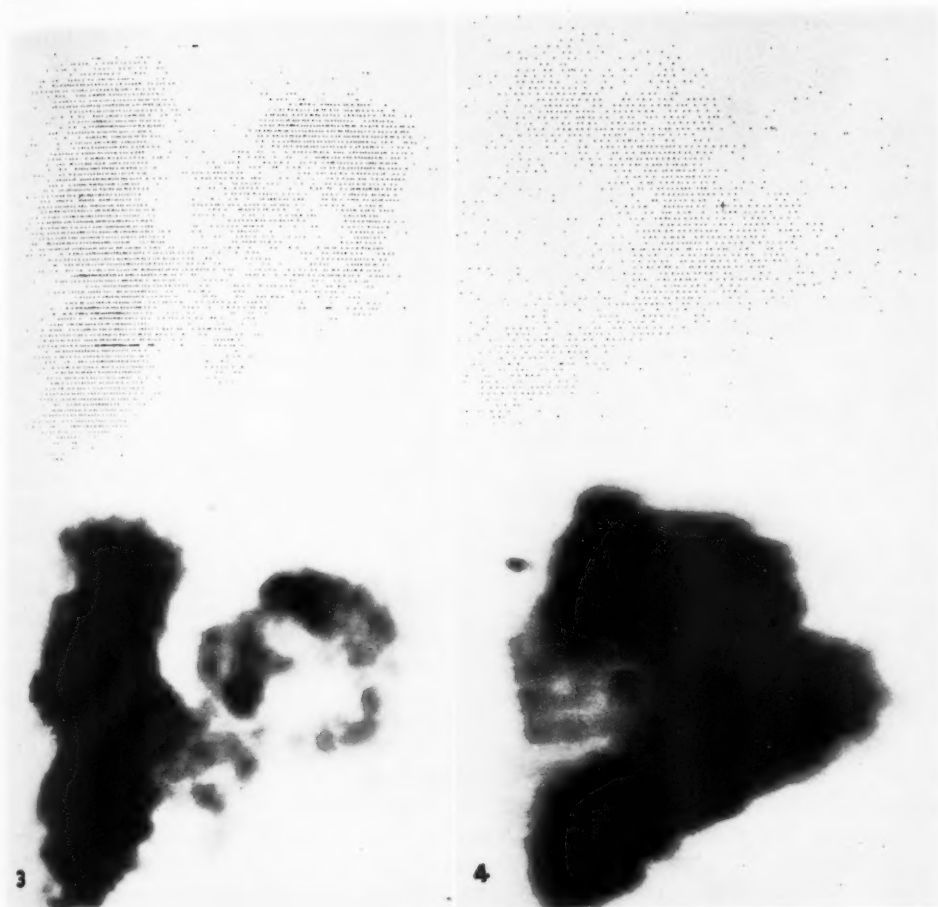


Fig. 3. Comparative hepatoscans recorded by simultaneous light recording and dot recording. Note variation in density range in left lobe of the film recording.

Fig. 4. Comparative hepatoscans recorded by simultaneous light recording and dot recording. Scatter of dots on upper scan is not seen on the film response since scattering is below threshold. The left lobe of the liver has been deliberately overexposed to show the dimensional effect of the invading mass in the right lobe.

detector head in reference to the  $x$  and  $y$  deflection axes of an oscilloscope. The  $z$  axis is modulated by the output from the detector so as to produce a visible record each time a count or a specified number of counts is recorded. The total effect of the dot distribution over the oscilloscope face is then recorded on film.

With this technic a wide range of accentuation of response has been obtained by modulation of the oscilloscope beam intensity. For a response linear with the counting rate, the oscilloscope beam intensity remains constant; so that the

greater exposure of the film at higher counting rates is due only to the greater superposition of dots by the oscilloscope beam per unit time. The intensity of each dot may also be modulated to increase non-linearly with the counting rate so that the increase in the latter produces a greater exposure of the film, not only because of the greater superposition of the dots, but also because each dot at the higher counting rate is individually more intense.

The primary disadvantage of conventional light recording is the narrow range

of effectiveness whereby a small increase in the counting rate may quickly saturate the film. This may not be undesirable under certain circumstances where the presence or absence of radioactivity is all that one wishes to record, but it is a distinct disadvantage when an effort is being made to reproduce on a scan all the varying levels of radiation which may be present in a large area or large volume. It is for this latter application that the oscilloscope technic has provided a satisfactory solution. By selection of maximum and minimum counting rates, the optimum accentuation of density with counting rate may be obtained. Without such a choice, a large measure of the advantage of light recording may be lost.

A comparison of both light recording and the conventional dot recording technic is shown in Figures 3 and 4, in which simultaneous liver scans were recorded by both methods.

Both of these recording systems involve data elimination or modification. This deliberate modification of data is necessary to their success since it is the elimination by cut-off circuit or accentuation by film response which makes visually perceptible small differences which might otherwise be overlooked or detected only by time-consuming and laborious methods. Thus the data become visually intelligible at the expense of a quantitative modification which is generally not significant. In the example shown in Figure 2 it is considered more important to determine that the nodule in the left lobe is not normal functioning liver tissue than to measure exactly the difference from the latter.

In most cases, it has been necessary to focus attention on small differentials in several ranges. For this reason it has been necessary to record two or three scans at differing cut-off or accentuation levels. Since the settings for the cut-off levels will influence the physical appearance of the scan itself, these levels become exceedingly important. Generally, the settings can be established by obtaining a rapid profile of the liver, but because of wide fluctuations in the anatomical configura-

tion it may be difficult to obtain the optimum setting for any given case.

In order to minimize the crucial nature of these settings, an electromagnetic tape recorder has been introduced to store permanently the signals obtained from the detector for later use. The signals recorded on the tape are then played back into the recorder at various accentuation or cut-off levels.

This system has four main advantages. (a) The settings applicable to one section of an organ may not give adequate differentiation or accentuation to another section; therefore, different settings may be required for various areas. (b) To obtain in every case optimum settings on the original scan, a laborious survey of the entire organ is required; multiple playbacks reduce the need for extreme care in these settings. (c) The effects of data modification may be easily recognized when scans are compared at different cut-off or accentuation levels. (d) Patient-handling time is reduced since, once the scan is recorded on tape, examination at various levels can be made merely by re-running the tape without the presence of the patient.

In the technic that we employ, the tape records all the counts detected, as well as the mechanical position of the detector head itself. The playback is then synchronized so that it reproduces identically the counts and position of the scintillation detector.

The effect of various cut-off levels on the appearance of a liver with uniform uptake of a radioactive material is shown in Figure 5. As the cut-off level increases, the outline becomes slightly smaller, since the thinner edge of the liver does not attain sufficient radioactivity to be recorded. In the 90 per cent cut-off level, artificial defects appear because the random fluctuation of counting rate exhibits levels that deviate 10 per cent or more from the peak counting rate. This accuracy is, of course, dependent upon both counting rate and time constant of the electronic control circuit. A clear understanding of this ex-

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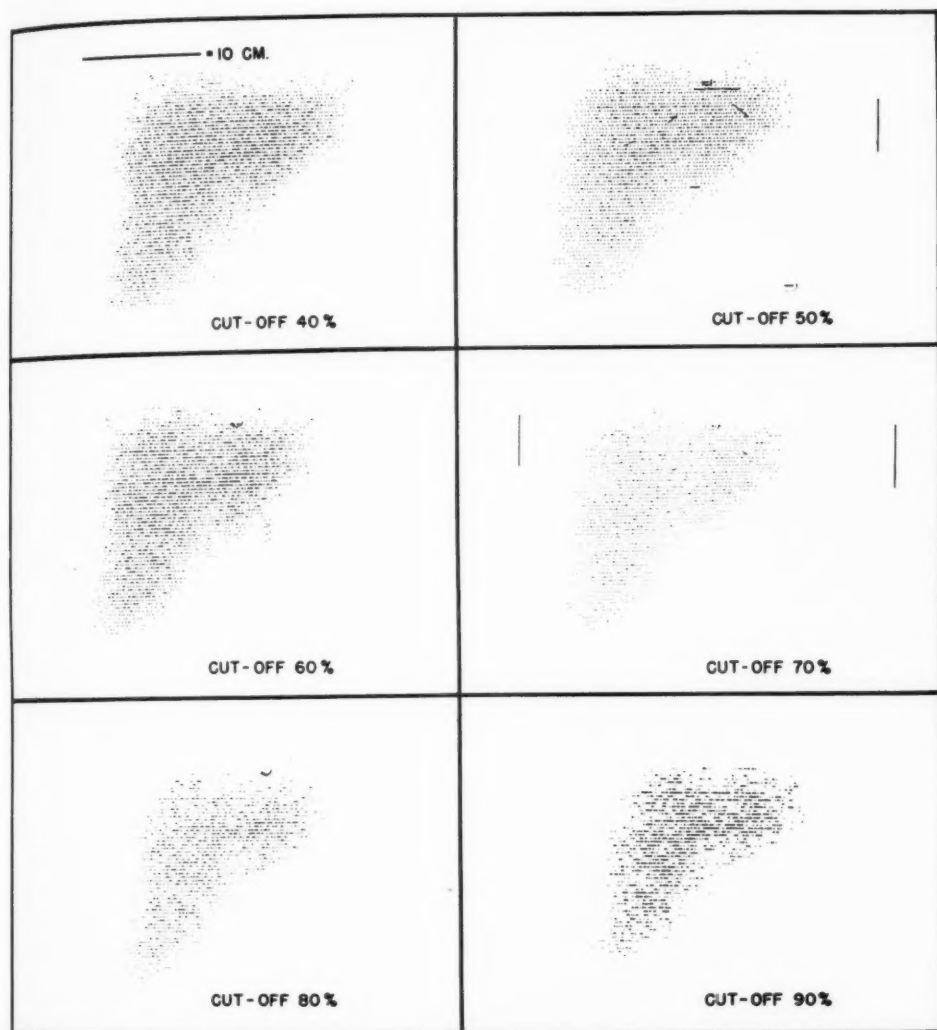


Fig. 5. Hepatoscan of liver with comparatively uniform uptake of colloidal gold<sup>1</sup> ( $\text{Au}^{198}$ ). Per cent levels of cut-off refer to ratio of cut-off level to the highest counting rate obtained over the liver. Note artificial defects occurring at 90 per cent level and general decrease of size with advanced cut-off settings.

pected variation is necessary for differentiation of artificial defects from real defects.

In Figure 6 a liver is shown with extremely low uptake in the left lobe. Original cut-off settings were placed to interrupt recording when the counting rate fell to less than 53 per cent and 35 per cent of the peak activity. Although these levels constitute reasonable settings that are applicable to many scans, the scans so recorded suggested a complete absence or

lack of function of the left lobe. Since the entire scan was recorded on tape, additional runs were made at different levels, which showed that the left lobe did exist and was functioning. They also showed clearly that the left lobe concentrated far less of the radioelement than the right. Without the playback feature, much of this information would have been missed.

A more gross dependence on cut-off levels is shown by the multiple scans of



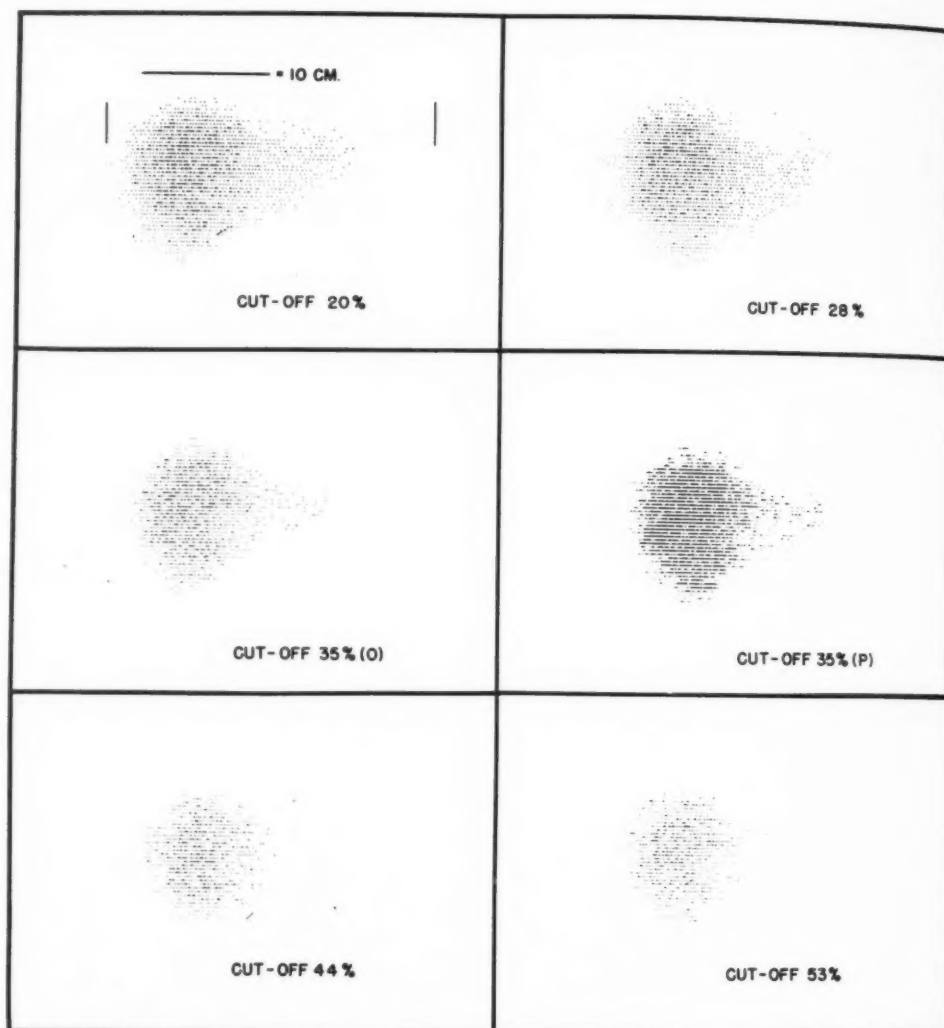


Fig. 6. Hepatoscan of liver with decreased uptake of  $\text{Au}^{198}$  in the left lobe. Center scans at 35 per cent cut-off levels show the original scan on the left (O) compared with a scan recorded by playback of the electromagnetic tape recorder at the same cut-off level on the right (P). Vertical lines at upper left refer to body margins.

Figure 7. This shows a liver invaded by large metastatic tumors and the organ exhibiting a wide variation of counting rates. The voids that appear in the 55 per cent cut-off level represent actual defects, since the variation greatly exceeds random counting error.

#### CLINICAL APPLICATION

Accentuation scintillation scanning techniques have been applied primarily to prob-

lems (a) of visualizing the structure of the liver following the administration of such materials as rose bengal ( $\text{I}^{131}$ ), tetraiodophenolphthalein ( $\text{I}^{131}$ ), and colloidal gold ( $\text{Au}^{198}$ ), and (b) of delineating the general configuration and position of various blood pools by the injection of iodinated ( $\text{I}^{131}$ ) human serum albumin. Detailed accounts of these techniques have been previously reported (3, 4, 5, 7), with some estimate of the accuracy of the method. The primary

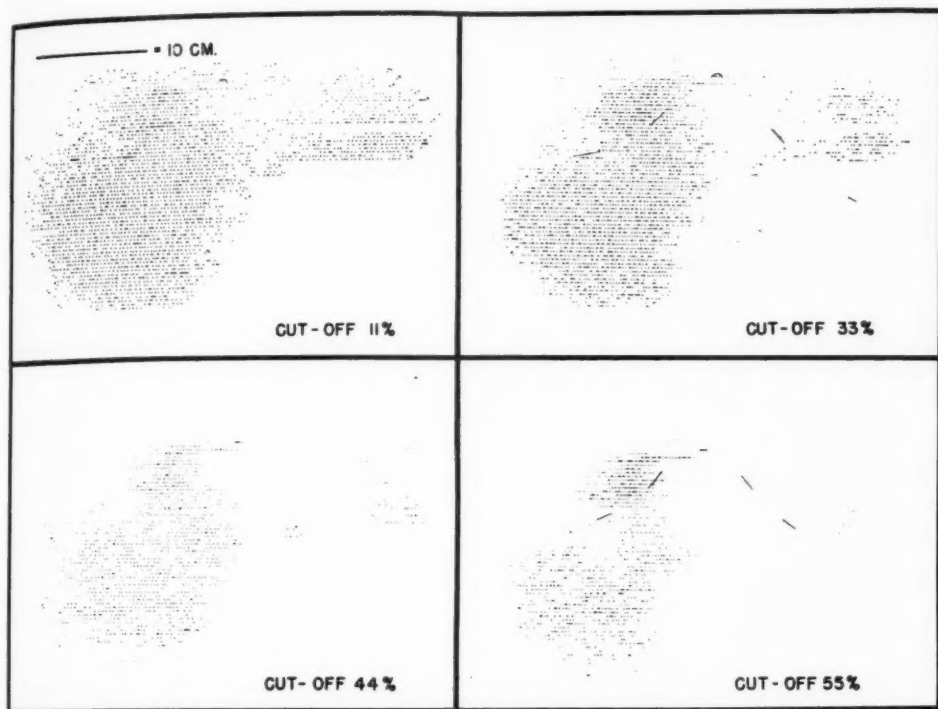


Fig. 7. Hepatoscan of liver with gross invasion by metastatic lesions. Note the large number of defects in the 44 per cent and 55 per cent cut-off levels even though the 33 per cent level appears uniform. This variation differs greatly from Fig. 5 wherein the relative uniformity is maintained up to 90 per cent of peak level.

modification in our approach has been a greater emphasis on the use of colloidal gold ( $\text{Au}^{198}$ ). This has certain practical advantages in that the gold is rapidly cleared from the blood and deposited in the liver and other reticuloendothelial tissue, thus permitting sharper delineation of the liver. Since the colloid remains relatively fixed in the liver, the dose may be given several hours previous to examination, the appearance of the scan being independent of time of injection within wide limits.

Previous efforts to identify metastatic nodules in the liver were made by the selection of radioelements which would be taken up in excess by abnormal tissue. Our approach was to select materials that would be preferentially absorbed by the normal liver tissue, observing the alteration produced by the tumor nodule. Such techniques have involved several complicating factors. First, rather than a complete ac-

cumulation of the radioactive material in the site under investigation, there is instead a general surrounding background of radioactivity always emanating from the patient. This background is due not only to the incomplete clearance of such materials as rose bengal and tetraiodophenolphthalein from the circulating blood but also to the fact that those materials, once accumulated by the liver, are excreted into the bowel through the common bile duct. Secondly, the size and depth of the liver make it difficult to obtain high differentials, since the detector must view a large segment of normal liver tissue both above and below any suspected abnormality or defect in the organ.

The success of these technics is dependent upon adequate visualization of small differentials. While most of the examples of liver visualization shown here have involved large masses of non-functioning liver

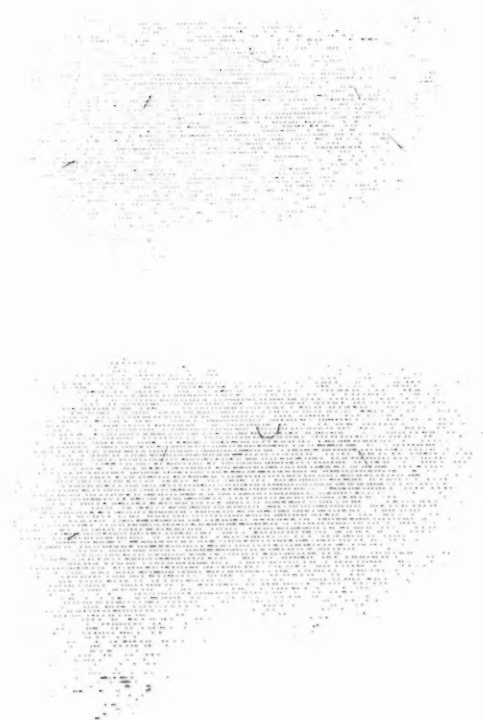


Fig. 8. Hepatoscan of cirrhotic liver obtained by administration of 200  $\mu$ c of colloidal gold ( $\text{Au}^{198}$ ). Defects at the lower cut-off (50 per cent) are perceptible but not readily visualized. The irregularities seen at the higher setting (70 per cent) may be considered as actual defects since they exceed random fluctuation at this counting rate.

tissue, this is not always the case in typical clinical problems. Figure 8, for example, shows a scan of a patient with cirrhosis, recorded at two cut-off levels. While the enlargement is obvious in both, it requires the higher cut-off to demonstrate adequately the many small defects present. These defects illustrate areas in which the counting rate has decreased to less than 70 per cent of the peak value, a level considerably below expected random fluctuation.

An additional example characteristic of the replacement of multiple small areas of functioning liver tissue is shown in Figure 9. In this case the many small defects due to carcinomatous nodules are adequately visualized, even though the actual size was



Fig. 9. Hepatoscan obtained with colloidal gold ( $\text{Au}^{198}$ ) showing multiple small nodules throughout the liver. Laparotomy exhibited many white soft nodules consistent with the scan and biopsy showed poorly differentiated adenocarcinoma.

minimal and the configuration and outline of the organ were relatively undistorted. Other instances of carcinomatous invasion of the liver which has been readily demonstrated by these technics are shown in Figures 2, 3, 4 and 7.

When these technics are applied to visualization of blood pools within the body, the primary information desired is not visualization of the pool itself but the demarcation between the pool and less vascular areas (7). It has been found that graphic illustration of cardiac blood pools and other large vascular channels is possible with a dose of 300 to 500 microcuries of iodinated ( $\text{I}^{131}$ ) human serum albumin. The size and configuration of the cardiac pool can now be compared with the cardiac shadow on conventional roentgenograms of the chest.

This technic is illustrated in Figures 10 and 11, which show roentgenograms of en-

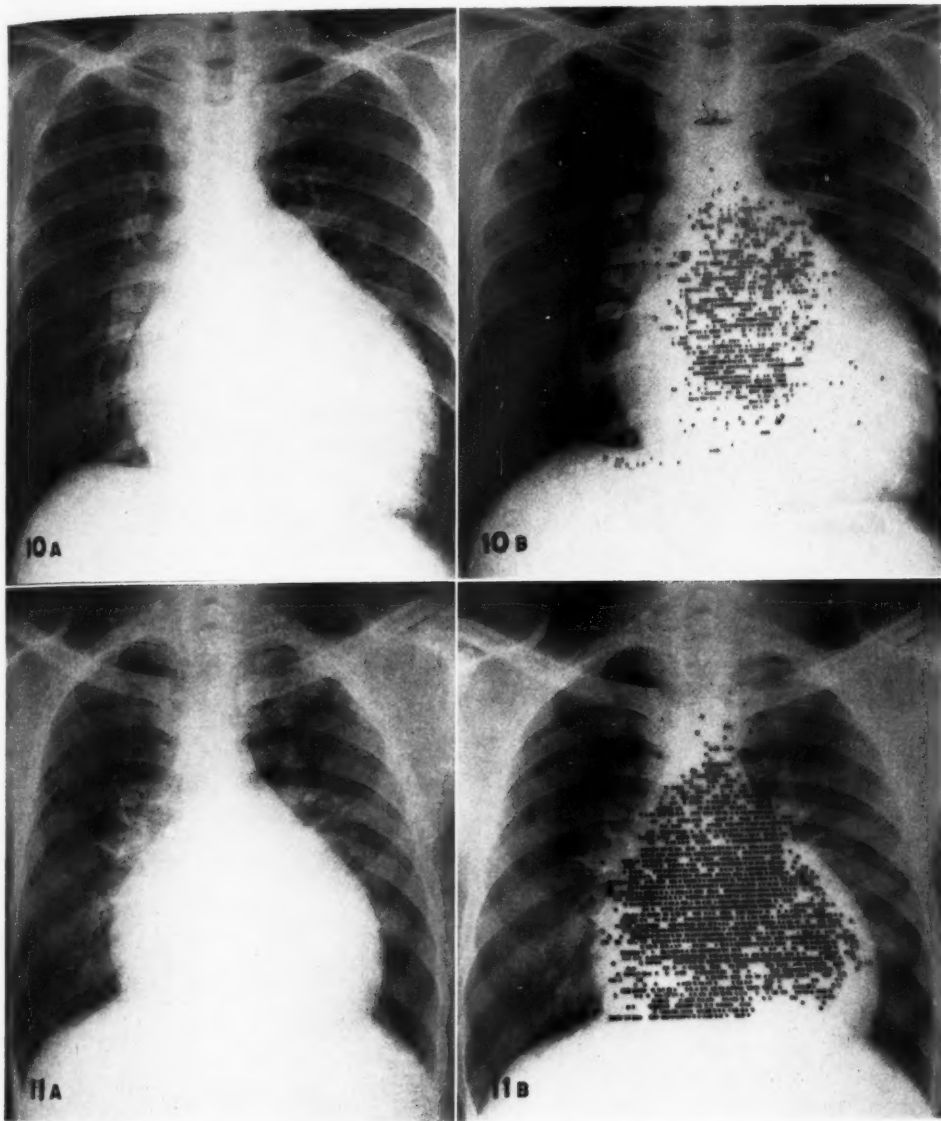


Fig. 10. A. Postero-anterior roentgenogram of chest of patient with an enlarged cardiac silhouette. B. Superimposition of scan of cardiac blood pool on roentgenogram indicates marked discrepancy between cardiac silhouette and blood pool, typical of pericardial effusion.

Fig. 11. A. Postero-anterior roentgenogram of chest showing enlarged cardiac silhouette. B. Superimposition of cardioscan on roentgenogram shows enlargement due to cardiac dilatation. (Patient discussed in detail in: Rejali, A. M., MacIntyre, W. J., and Friedell, H. L., *Am. J. Roentgenol.* 79: 129, 1958.)

larged cardiac silhouettes. By means of the superimposed cardioscan it has been determined that the enlargement in Figure 10 is due to a pericardial effusion, since only the central area contains a high concentration of the radioactive material. In Figure

11, however, suspected pericardial effusion has been ruled out since the cardioscan shows that almost all of the enlarged area is part of the circulating blood pool.

The differentiation of mediastinal masses from aneurysms is illustrated in Figures 12

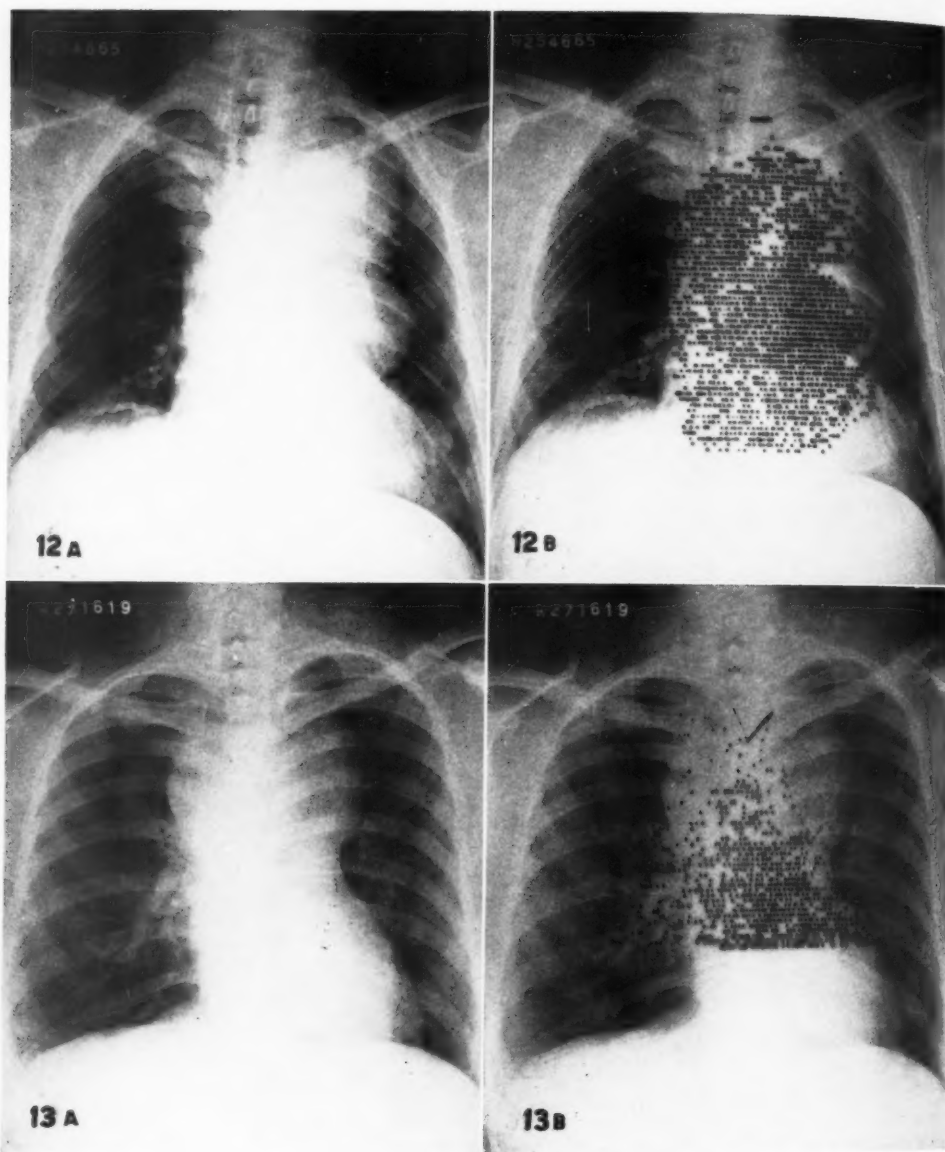


Fig. 12. A. Postero-anterior roentgenogram of chest of patient with unusual widening of the mediastinum. B. Superimposed cardioscan corresponds with the mediastinal mass, consistent with aneurysm of the aorta. (Patient discussed in detail by Rejali, A. M., MacIntyre, W. J., and Friedell, H. L., *Am. J. Roentgenol.* 79: 129, 1958.)

Fig. 13. A. Postero-anterior roentgenogram of chest with mediastinal widening similar to previous figure. B. Lack of correspondence of mass with blood pool scan is inconsistent with aneurysm of aorta. Mass later proved to be due to Hodgkin's disease.

and 13. The unusual widening of the mediastinum in Figure 12 is due to aneurysm of the aorta. This is consistent with the superimposition of the large blood pool

visualized by the cardioscan, which corresponds to the position of this increase. In Figure 13, the roentgenogram shows similar mediastinal widening, but it was possi-

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ble to show by scanning that no large blood pool was present and an aneurysm could be reasonably excluded. This mediastinal mass was later proved to be due to invasion by Hodgkin's disease. In this scan only the upper portion of the heart had been studied since this was the only region where differentiation of blood pools from avascular regions was required.

#### DISCUSSION

The visualization of any organ, tissue, or internal structure by means of a radioisotope scanner is contingent upon a variation in the uptake of radioactive material between the site of interest and its environment. When this differential is not large, it becomes necessary to consider some type of accentuation technic that would make the difference readily perceptible. It should be clear that such systems are never a substitute for the most effective collimation procedures and the best types of detection. They are designed merely to enhance and make quickly intelligible the information obtained by the differential deposition of radiation-emitting elements.

As with any system of data modification, care must be exercised both in the selection of accentuation parameters and the interpretation of records obtained. Information in many cases has been reduced to the identification of areas exhibiting deposition of radioactive material either greater or less than a specified level.

For this reason we feel that multiple recordings are necessary to obtain the full advantages of this system. While we have previously obtained three simultaneous scans for each patient, this may not be the optimum number. In addition, a standard set of accentuations or cut-off levels may not be adequate for all cases because of the wide individual variance in the deposition of radioactive material. If such a standard set of levels cannot be derived, the use of the electromagnetic tape recorder with multiple playbacks may well be a most important adjunct to such technics. The use of such a device greatly minimizes the experience necessary for the operator, per-

mits a permanent record which can be examined repeatedly, and with one sitting provides innumerable scans which can be reproduced at various cut-off levels in order to establish more effectively abnormalities in the general configuration and structure of the region under study.

#### SUMMARY

1. A counting rate cut-off circuit and a light-recording accentuation technic have been utilized for the visualization of small differences in the uptake of radioactive material by the liver and by various blood pools.

2. Examples are shown of the use of these technics to emphasize the invasion of the liver by both benign and neoplastic processes, the separation of pericardial effusion from cardiac enlargement or dilatation, and the differentiation of mediastinal masses from aneurysm of the aorta.

3. The need of multiple levels in this technic is stressed, and the application of an electromagnetic tape recorder for this purpose is described.

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## SUMMARIO IN INTERLINGUA

## Le Visualisation de Organos Interne per Medio de Technicas de Scrutation Scintillatori a Accentuation

Duo systemas de registration esseva disveloppate pro accentuar micre differentias inter le nivellos del acceptation de radioisotopos in areas adjacente intra le region scrutate. Le prime de iste systemas introduce un circuito de interruption controlate que permette le selection arbitrari de un nivello de contation infra le qual nulle punctos es registrate. Le secunde es equipate a augmentar le responsa a plus elevate nivellos de activitate per medio de un systema de registration luminar con le effecto de un accentuation de micre differentias inter le nivellos de contation.

Ambe iste systemas de registration labora con le elimination o modification del datos. Isto representa in ambes le condition essential de lor successo, proque il es le elimination per le circuito interruptori o le accentuation per le responsa luminar que rende visualmente perceptibile un classe de micre differentias que alteremente

escapparea al detection o poterea esser detegite solmente per methodos costose in tempore e effortio. Pro reducer le importantia critic del adjustment del machina, un registrator electromagnetic es utilisate. Isto registra permanentemente le signales obtenite ab le detector, de maniera que repetite reproductiones deveni possibile con varie nivellos de accentuation e de interruption. Le banda magnetic responde a omne le signales percipite per le detector e etiam al position mechanic del capite del detector mesme.

Le illustrationes includite monstra le effecto de varie nivellos de interruption, in le caso del prime methodo, super un scrutinio de hepate con acceptation uniforme del material radioactive e le effecto del secunde technica in le demarcation inter massas de sanguine e areas minus concentratemente vascular in le differentiation de effusion pericardial, aneurysmo, e morbo de Hodgkin mediastinal.



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# Use of the TSH Test in the Diagnosis of Thyroid Disorders<sup>1</sup>

WILLIAM McK. JEFFERIES, M.D., RICHARD P. LEVY, M.D., and JOHN P. STORAASLI, M.D.

THE MEASUREMENT of the uptake of a tracer dose of  $I^{131}$  by the thyroid gland has become a standard test of thyroid function. When combined with the basal metabolic rate (BMR) and determination of serum protein-bound iodine (PBI), it gives the clinician a more complete picture of thyroid activity than has ever before been available. Yet there are circumstances in which all three of these tests are inadequate. In such instances it is neces-

sumarizes its usefulness as a diagnostic tool, based on more than 1,000 tests performed in the last six years.

## TECHNIC

The technic of the test has changed little since the first report (1). The schedule remains the same (Fig. 1). The entire test requires but two half-days, and the subjects may be ambulatory. On the morning of day 1, a tracer of 8 microcuries

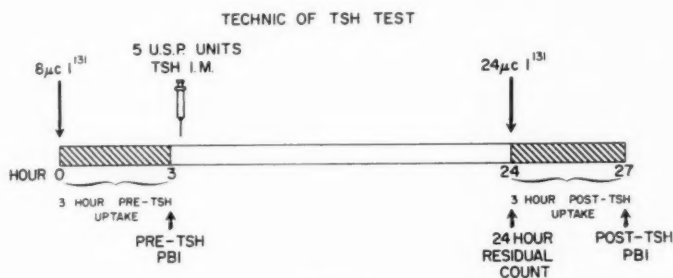


Figure 1.

sary to determine the response of the thyroid gland to stimulation in order to detect an abnormality in its function.

For this purpose an additional test is needed, and the TSH test meets the requirements. By following the response of the thyroid uptake of  $I^{131}$  and the PBI to a single injection of thyrotropin (TSH), the ability of the thyroid gland to respond to stimulation can be determined in a satisfactory and practical manner. Previous reports from this clinic (1, 2) have dealt with the value of this test in the diagnosis of obscure hypothyroidism and low thyroid reserve. The present report

of  $I^{131}$  is given orally.<sup>2</sup> Although it was initially recommended that the subject be fasting, it has been found that a light breakfast will not interfere significantly with the three-hour uptake since the delaying action of food upon the absorption of iodide lasts less than an hour (3). Three hours after administration of the tracer dose the thyroid uptake of  $I^{131}$ , corrected for background, is measured and a blood specimen is drawn for a PBI determination. These are the pre-TSH three-hour  $I^{131}$  uptake and PBI values. Five units of TSH<sup>3</sup> are then injected intramuscularly. Twenty-four hours after the administra-

<sup>1</sup> From the Departments of Medicine and Radiology, Western Reserve University School of Medicine and University Hospitals of Cleveland, Ohio. This investigation was aided by grants from the Institute of Arthritis and Metabolic Diseases of the National Institutes of Health, U.S. Public Health Service (PHS Grant A 565) and the Hankins Foundation, and was supported in part by A.E.C. contract W31-109-eng-78 with Western Reserve University.

Presented, as part of a Symposium on The Use of Isotopes in Diagnosis, at the Forty-fourth Annual Meeting of the Radiological Society of North America, Chicago, Ill., Nov. 16-21, 1958.

<sup>2</sup> Smaller tracer doses are employed for children.

<sup>3</sup> The Armour Laboratories have generously supplied the TSH (Thytropar) used in these studies.

TABLE I: RESPONSE TO THE TSH TEST IN NORMAL SUBJECTS

Thyroidal 3-hr. $I^{131}$ Uptake*			Serum PBI†			Thyroidal 24-hr. $I^{131}$ Uptake*
Pre-TSH	Post-TSH	Change	Pre-TSH	Post-TSH	Change	
10.1±4.1	30.5±9.6	+20.4±7.8	5.8±1.0	8.9±1.7	+3.1±1.1	29.3±6.3

\* Expressed as the mean and standard deviation of the percentage of the tracer dose counted over the thyroid gland, corrected for background and physical decay.

† Expressed as the mean in micrograms per 100 ml. with standard deviation.

tion of the first tracer another count is made over the thyroid gland to determine the residual radioactivity and then a larger tracer, 24 microcuries,<sup>2</sup> is given. Three hours after this, the thyroid uptake of the second tracer is determined by correcting the total count over the gland for background and the residual of the first tracer, with allowance for its physical decay over the three-hour period. A second blood specimen is drawn for PBI determination. These are the post-TSH three-hour uptake and PBI values. The differences between these and the pre-TSH values indicate the response of the thyroid, a rise in  $I^{131}$  uptake reflecting an increased rate of iodide-trapping, and an increase in PBI, the release of hormone from the gland (2). The use of a larger tracer dose on day 2 lessens the possible error caused by the necessity of correcting the three-hour count for the residual of the first tracer.

The schedule of this test has several advantages. The three-hour uptake gives a better indication of the rate of uptake of iodide by the thyroid than a longer interval, and yet is sufficient to avoid errors resulting from differences in rate of absorption that might occur with a shorter period. It has also been shown that the greatest effect of a single dose of TSH on both the rate of iodide uptake and the level of PBI occurs twenty-four hours after its injection. Furthermore, the interval is convenient for both the laboratory and the patient, making possible completion of the test in little more time than is required for a twenty-four-hour uptake study. Except in rare circumstances, the count over the thyroid at twenty-four hours, to determine the residual of the first tracer, has been found not to differ significantly from the customary twenty-four-hour  $I^{131}$  uptake without TSH. The reason for this is

that TSH does not begin to increase the rate of uptake of iodide until eight hours after its intramuscular injection, and by this time, eleven hours after the administration of the first tracer, the distribution of the isotope between the thyroid gland and the kidneys is for the most part complete.

The normal response to the test, with standard deviations, is presented in Table I. In a series of euthyroid hospital patients given  $I^{131}$  tracers according to the schedule of the test, but without the administration of TSH, it has been found that approximately 10 per cent have sufficient discrepancy between the three-hour uptakes on two successive days to obscure the effect of TSH, but in such instances the PBI levels will usually indicate the true status of thyroid function (4). Exposure to inorganic iodide will of course invalidate  $I^{131}$ -uptake measurements, and organic iodides such as those used as radiopaque media invalidate both the  $I^{131}$ -uptake and serum-PBI determinations.

No serious side-effects of TSH administration have been encountered. An occasional mild, transient, inflammatory reaction has been observed at the site of injection, and moderate urticaria has occurred in 4 subjects, with every case responding to antihistaminics.

#### APPLICATIONS

From a clinical standpoint, the ability of the TSH test to determine the potential function of a thyroid gland while the host is taking thyroid medication is one of its most valuable attributes. Whether a patient who has been taking thyroid medication for some time really has hypothyroidism when first seen is a relatively common clinical problem. Customary tests, such as the BMR, PBI, and  $I^{131}$  up-

TABLE II: RESPONSE TO THE TSH TEST OF A PATIENT RECEIVING THYROID MEDICATION (PATIENT R. D., 59-YEAR-OLD FEMALE)

Date	Thyroidal I <sup>131</sup> Uptake (per cent of Tracer Dose)			Serum PBI (mcg./100 ml.)		Treatment
	Pre-TSH (3-hr.)	Post-TSH (3-hr.)	24-hr.	Pre-TSH	Post-TSH	
3/16/54	3	26	14	6.1	7.2	Thyroid 0.2 gm./day for 20 + years
2/7/55	11	36	32	6.0	8.2	No thyroid since 6/1/54

TABLE III: RESPONSE TO THE TSH TEST OF PANHYPOPITUITARISM VERSUS PRIMARY HYPOTHYROIDISM

Test No.	Diagnosis	Thyroidal I <sup>131</sup> Uptake (per cent of Tracer Dose)			Serum PBI (mcg./100 ml.)	
		Pre-TSH (3-hr.)	Post-TSH (3-hr.)	24-hr.	Pre-TSH	Post-TSH
132	Panhypopituitarism	6	20	31	1.7	4.2
231	Primary hypothyroidism	7	9	5	1.1	1.4

TABLE IV: RESPONSE TO THE TSH TEST OF A PATIENT WITH LOW THYROID RESERVE

Test No.	Diagnosis	Thyroidal I <sup>131</sup> Uptake (per cent of Tracer Dose)			Serum PBI (mcg./100 ml.)		Serum Cholesterol (mg./100 ml.)
		Pre-TSH (3-hr.)	Post-TSH (3-hr.)	24-hr.	Pre-TSH	Post-TSH	
190	? Hypothyroidism (I <sup>131</sup> for Graves' disease six months previously)	12	12	22	4.2	4.1	380

take are not helpful because of the ingestion of thyroid. Many such patients are convinced that they need this medication, and even if they can be persuaded to discontinue it, months of observation may be required to determine whether their thyroids are capable of normal function, since, after a period of suppression by exogenous medication, the gland may be slow in recovering. Through the use of the TSH test, the potential capabilities of such glands can be quickly determined without interruption of thyroid administration. After suppression by large doses of exogenous thyroid for many years, the rate of iodide uptake is capable of a rapid response to TSH stimulation, as reflected in a significant increase in the three-hour uptake of the second tracer compared with that of the first. Because such glands are usually depleted of stored hormone after prolonged suppression, and because the rise in PBI with the schedule of the test reflects release of stored hormone, this part of the study is of little value in such cases and can be omitted. The response to the

TSH test of a 59-year-old woman who had been taking 0.2 gm. thyroid daily for over twenty years is presented in Table II.

In panhypopituitarism the status of thyroid function is similar to that of patients who have been on suppressive doses of thyroid medication for a prolonged period, in that both conditions are associated with a deficiency of endogenous TSH. Since patients with the former disorder respond to TSH in a manner similar to those receiving exogenous thyroid, the TSH test is helpful in distinguishing between primary thyroid failure and hypothyroidism secondary to pituitary insufficiency. In Table III the response of a patient with panhypopituitarism is contrasted with that of a patient with primary hypothyroidism.

Another more common clinical condition in which the TSH test may be valuable is mild hypothyroidism or low thyroid reserve. This disorder occurs when the thyroid gland is partially destroyed by thyroiditis or I<sup>131</sup> therapy, or has been subtotally removed by surgery, and the remaining tissue is functioning at a maximum



TABLE V: ABNORMAL RESPONSES TO THE TSH TEST IN TWO PATIENTS WITH NON-TOXIC DIFFUSE GOITERS

Test No.	Thyroidal I <sup>131</sup> Uptake (per cent of Tracer)			Serum PBI (mcg./100 ml.)	
	Dose		24-hr.	Pre-TSH	Post-TSH
	Pre-TSH (3 hr.)	Post-TSH (3-hr.)			
338	18	19	28	6.3	8.4
362	11	39	29	4.9	5.3

rate from stimulation by endogenous TSH. I<sup>131</sup> uptake and PBI may be within the normal range, yet the patient may have mild, sometimes intermittent, symptoms of hypothyroidism, occasionally associated with hypercholesterolemia (Table IV). Presumably the remnant is unable to meet fully the body's requirement for hormone despite the normal PBI. In such cases the TSH test clearly indicates the nature of the disorder through the lack of response to stimulation, and appropriate thyroid therapy relieves the symptoms and hypercholesterolemia.

Another situation where the TSH test may indicate an abnormality of thyroid function in the presence of an I<sup>131</sup> uptake and PBI within normal limits occurs in some cases of non-toxic diffuse goiter. The I<sup>131</sup> uptake or PBI, or both, may fail to respond normally to stimulation, indicating a defect in thyroid function that is presumably related to the development of the goiter (Table V). Such glands frequently return to normal size with appropriate doses of desiccated thyroid. In at least some of these cases struma lymphomatosa is demonstrated at biopsy.

## SUMMARY

The TSH test has proved a satisfactory and practical means of determining the ability of the human thyroid gland to respond to stimulation. Because of this property it is a valuable diagnostic aid in determining potential thyroid function in patients receiving thyroid medication, in demonstrating the presence of low thyroid reserve in mild cases of hypothyroidism or abnormal thyroid function in some patients with non-toxic diffuse goiters, and in distinguishing between primary thyroid failure and hypothyroidism secondary to pituitary insufficiency. Because the PBI response measures release of stored hormone, it may be of little help in testing patients on thyroid therapy and in distinguishing secondary hypothyroidism, but in other instances it should be determined in addition to the change in thyroidal I<sup>131</sup> uptake in order to obtain a more complete picture of thyroid function.

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## SUMMARIO IN INTERLINGUA

### Le Uso del Test de Hormon Thyroido-Stimulante (HTS) in le Diagnose de Disordines Thyroide

In certe situationes, le test a I<sup>131</sup> traciator, le test de iodo ligate a proteina, e tests del metabolismo basal es inadequate pro le diagnose de disordines thyroide. Un altere procedimento, mesurante le responsa del thyroide al stimulation per thyrotropina, HTS, ha essite usate per le autores con satisfacente resultatos in plus que mille casos in le curso del passate sex annos.

Le test a HTS es utile in le determination del potential de function thyroide in patientes qui recipe medicina, in le demonstration del presentia de basse reservas thyroide in leve casos de hypothyroidismo o de dysfunction thyroide in certe patientes con struma non-toxic, e in le distinction inter primari disfallimento thyroide e hypothyroidismo secundari a insufficientia pituitari.

## Some Clinical Aspects of Isotope Circulation Studies<sup>1</sup>

RICHARD H. GREENSPAN, M.D., RICHARD G. LESTER, M.D., JAMES F. MARVIN, Ph.D., and KURT AMPLATZ, M.D.

**R**APIDLY ADVANCING technics in the surgical repair of congenital cardiac lesions have made precise preoperative diagnosis a matter of great importance. The site of the defect and its hemodynamic behavior must be determined with accuracy, since operative approaches and bypass procedures vary widely with lesions in different locations. Diagnosis depends on close cooperation between the clinician, radiologist, and physiologist. Each of these must have information from the others in order to evaluate his findings correctly and completely, and each must have some general knowledge of all three fields. Newer knowledge of the normal variations and pathologic lesions provided by the surgeon and pathologist, combined with advances in radiologic technics, have greatly increased the importance of the radiologist as a member of the diagnostic team. The present authors have developed a method for aid in diagnosis which is in the realm of the radiologist, employing radioisotopes as a physiologic tool for the detection and location of intra- and extracardiac shunts (1, 2).

Left-to-right shunts can usually be detected by use of the cardiac catheter and determination of the oxygen content of blood samples withdrawn from the various chambers and vessels. Variations in pressure will reveal stenotic or obstructed sites. Right-to-left shunts are, however, considerably more difficult to pinpoint. Dye dilution with the use of Evans blue, or more recently Fox green, is a reliable and precise procedure. For most accurate results, however, arterial puncture and the placing of an indwelling arterial catheter are required (3). This procedure is fairly

easy to accomplish in the adult, but is difficult in the infant and young child, and at the University of Minnesota Hospitals a large percentage of the patients seen for catheterization are under five years of age. Also, since our catheterizations are done under local anesthesia, we are interested in producing the least trauma to the patient and avoiding the changes in circulatory dynamics that occur secondary to struggling and crying. An additional drawback to dye dilution methods consists of the need for highly trained personnel to insure accurate results.

Selective angiocardigraphy, with injection at the time of catheterization, is being used with greater frequency as rapid film-changing devices and cine-equipment become more reliable. Small shunts, however, may be missed due to rapid dilution of the opaque material by non-opacified blood as it traverses the shunt. The volume required for good visualization frequently may be such that unusual pressure is produced in the injected chamber, and a misleading right-to-left shunt may be produced where one does not actually exist in the physiologic state. In addition, although significant advances have been made in increasing the safety of contrast media, there is still some inherent danger in the injection of large amounts of iodinated compounds.

The technic developed by the authors consists of the injection of trace amounts of  $I^{131}$ -labeled Renografin, either directly into the arm or through the cardiac catheter into various chambers and vessels, and the detection of appearance times and slopes by means of externally placed collimated scintillation counters.

<sup>1</sup> From the Department of Radiology, University of Minnesota, Minneapolis, Minn. Supported in part by the Graduate School, University of Minnesota, Minneapolis, Minn., and by E. R. Squibb & Sons, through the Squibb Institute for Medical Research, New Brunswick, N. J.; in part by U.S.P.H.S. Grant No. H-3580.

Presented, as part of a Symposium on The Use of Isotopes in Diagnosis, at the Forty-fourth Annual Meeting of the Radiological Society of North America, Chicago, Ill., Nov. 16-21, 1958.

## METHODS

$I^{131}$ -labeled Renografin<sup>2</sup> is supplied to us in sterile form with activity of 300 to 400 microcuries per cubic centimeter. Approximately 1 microcurie per kilogram of body weight is used for the initial injection (50 microcuries for the average adult). Second and third injections require doubling and tripling the initial dose to produce enough counts above body background for accurate detection. The radioactive ma-

be individually adjusted to the height desired. The counters include  $1 \times 1$ -in. thallium-activated sodium-iodide crystals and are shielded by a minimum of 1 in. of lead (Fig. 1). Just prior to the injection they are rolled into position and are held over the precordium and a major artery. Initially, the femoral artery was used as the peripheral vessel. A much larger volume of blood, however, flows in the abdominal aorta, and sensitivity of pick-up is sig-

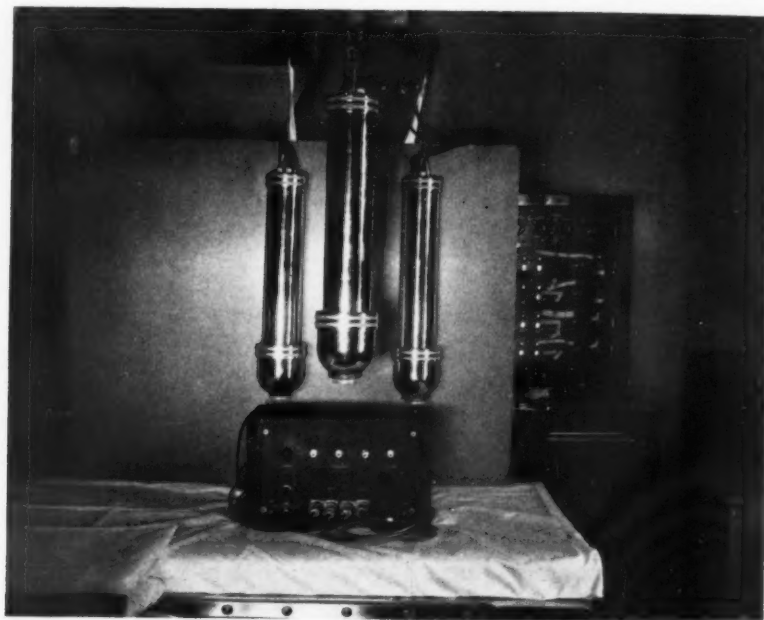


Fig. 1. Shielded counters, power supply, ratemeters, and Polyviso recorder.

terial is pre-mixed with a small volume of stable Renografin in order to increase its specific gravity. It is then layered in a syringe in front of 5 cc. of saline and rapidly injected into the catheter when the study is performed.

Collimated, shielded scintillation counters are suspended by cables from a metal frame which travels in the supporting track for the Westinghouse Image Intensifier used during the catheterization. A spring suspension permits each counter to

nificantly greater in that vessel. Proper shielding is, of course, imperative, especially when the peripheral vessel is so close to the precordium. A third counter has been utilized over the lung in a series of patients.

The great majority of our studies have been accomplished at the time of catheterization, injection being made through the cardiac catheter. Injection by direct venopuncture has been done, however, in adults, as a screening method for the detection of shunts, with good results. A large-bore needle (No. 18) is necessary in order to introduce a good bolus of radio-

<sup>2</sup> Kindly prepared for and supplied to us by E. R. Squibb and Sons, through the Squibb Institute for Medical Research, New Brunswick, N. J.

active material, and the placing of such a needle usually is not practical in infants and young children.

Special instrumentation has been developed for these studies. Since information must be collected over relatively short periods, ratemeters with short time constants (a half to one second) are essential.

The amplifier, multivibrator, and rate-meter circuits are fully transistorized. They represent a single plug in the main unit, which also includes the low-voltage power unit and a hermetically sealed 1,500-volt regulated transistorized high-voltage source (Fig. 2). The preamplifiers are mounted with the photomultiplier tubes in the shielded section of the counters, and the ratemeters were designed to connect directly to the Sanborn Polyviso recorder.

Linear circuits were used initially. This type of integration, however, was found unsuitable for congenital heart studies, since the counting rates that will occur cannot be accurately predicted. Since the short duration of the entire procedure precludes sensitivity adjustments during the study, all controls must be pre-set. The circuits finally adopted provide non-linear recordings closely approximating a logarithmic two-octave scale.

In cases where more than one injection is being made, recording of residual radioactivity in the body is suppressed by changing the time constant of the storage circuit. A switch is provided for this on the control panel.

#### RESULTS

When injection is made through the cardiac catheter the precordial counter records an immediate sharp rise in activity. If a peripheral vein is injected, the rise will be delayed a few seconds. One to two heartbeats later the material is detected by the counter held over the peripheral lung field. If the cardiac (precordial) counter is sharply collimated, a slight decrease in activity will be observed while the isotope is in the lungs. This is followed by another increase in activity, and then a decline to equilibrium.

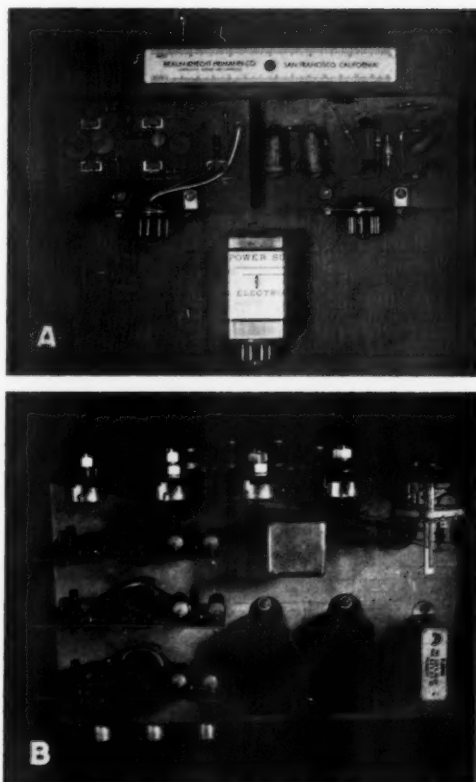


Fig. 2. A. Transistorized plug in ratemeters and power supply.  
B. Open view: Ratemeters and power supply.

In the normal subject (Figs. 3 and 4), the collimated counter over the peripheral artery then records a precipitous rise, followed by a slight decrease in activity before equilibrium is reached. Heart-to-aorta or heart-to-femoral-artery interval varies between five and twelve seconds, and depends partly on cardiac rate. We have found heart-to-femoral-artery intervals of between 8 and 18 heartbeats in normal controls. No significance is attached to the down-slope of the peripheral artery curves, since the counter placed over the aorta or upper leg is recording radioactivity from the veins and capillaries as well as from the artery.

Right-to-left shunts are characterized by a short interval between appearance of the radioactive material at the heart and its

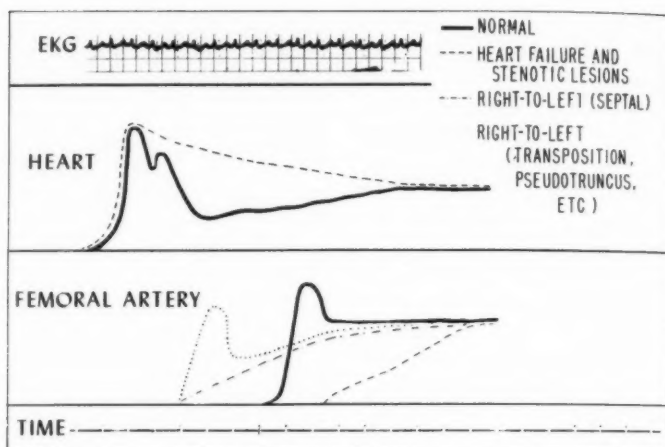


Fig. 3. General patterns.

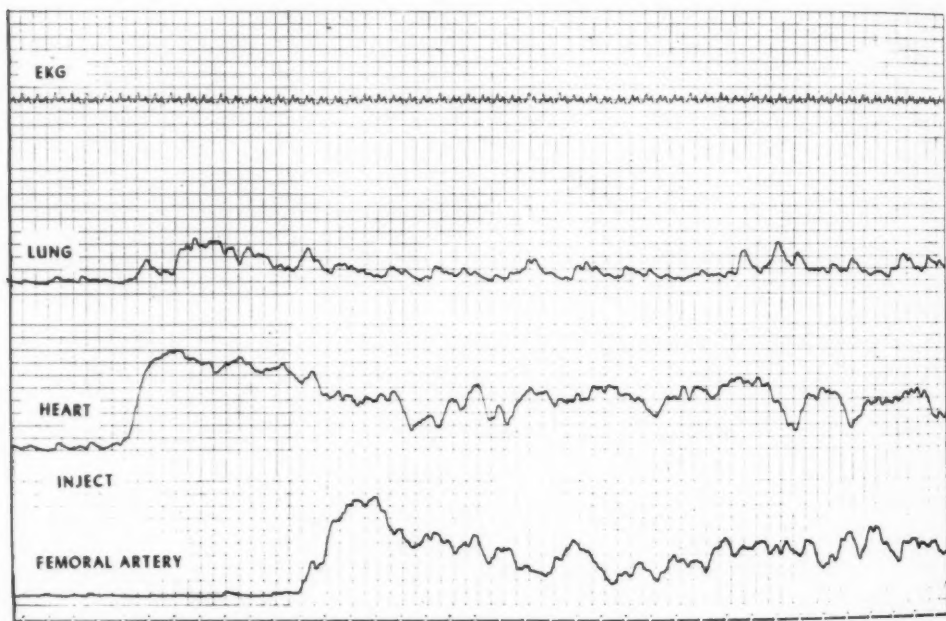


Fig. 4. Normal study: Seven-second heart-to-peripheral-artery interval.

appearance at the peripheral artery, as the isotope-containing venous blood is shunted into the systemic circulation (Figs. 3 to 5). In grossly cyanotic patients with transposition of the great vessels, pseudotruncus, and tetralogy of Fallot, there is an early appearance of a large radioactive bolus at the peripheral vessel, since a consider-

able portion of the systemic cardiac output consists of desaturated blood. The duration of high counts from the precordial detection is short (Fig. 5).

In patients with smaller right-to-left shunts, most frequently septal, radioactivity makes an early appearance, as in the grossly cyanotic group, but the amount



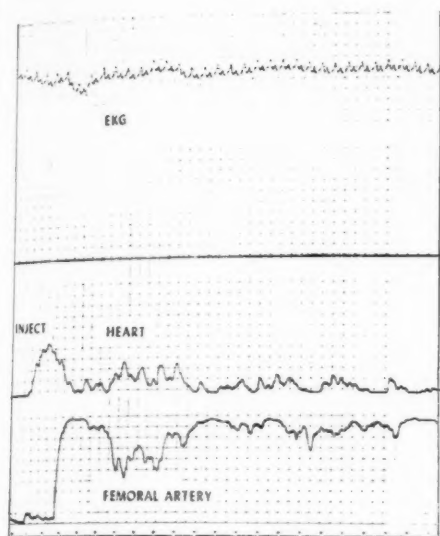


Fig. 5. Cyanotic tetralogy of Fallot: Two-second heart-to-femoral-artery interval.

Location of the right-to-left shunt is determined by making multiple injections into various chambers. The most distal chamber or vessel that, when injected, will produce early appearance of radioactivity at the femoral artery is the site of the right-to-left shunt. In a cyanotic boy in whom no diagnosis was possible by cardiac catheterization and angiocardiology, an isotope injection was made into the right ventricle. Five seconds later, radioactivity appeared at the femoral artery (normal time) (Fig. 7, A). The catheter was then withdrawn to the right atrium and, upon reinjection, a two-second interval between the appearance of radioactivity at the heart and at the femoral artery was recorded (Fig. 7, B), affording clear evidence of a right-to-left shunt at the atrial level. We have had 5 such cases of trilogy of Fallot with isotope diagnosis.

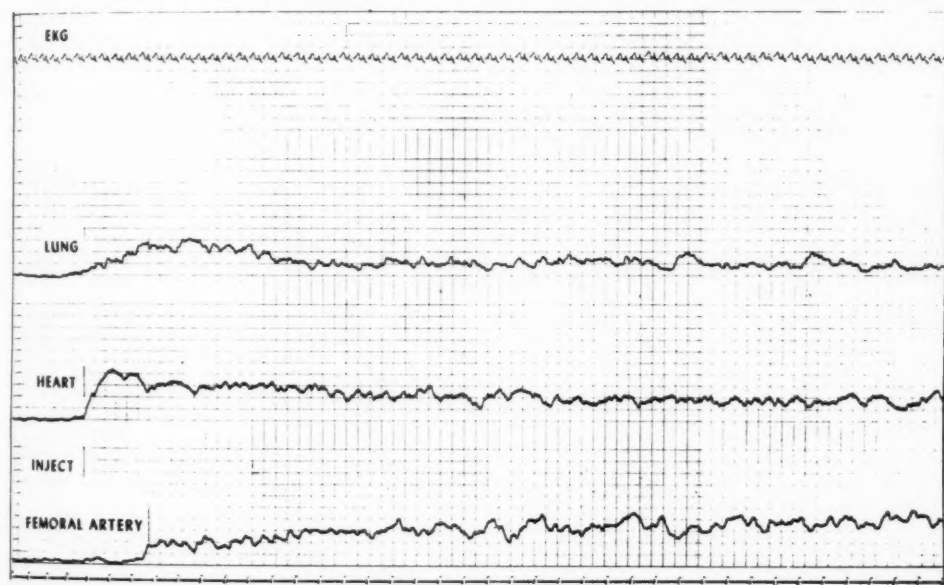


Fig. 6. Single ventricle: Appearance interval of two and a half seconds; gradually increasing peripheral artery activity.

is small and variable, and a shallow slope is often seen over the peripheral artery (Figs. 3 to 6). These defects are frequently, although not necessarily, associated with left-to-right shunts.

Typical patterns of the precordial records for the various anatomic malformations producing right-to-left shunts have not been noted. It is possible that a few of the more common anomalies in this

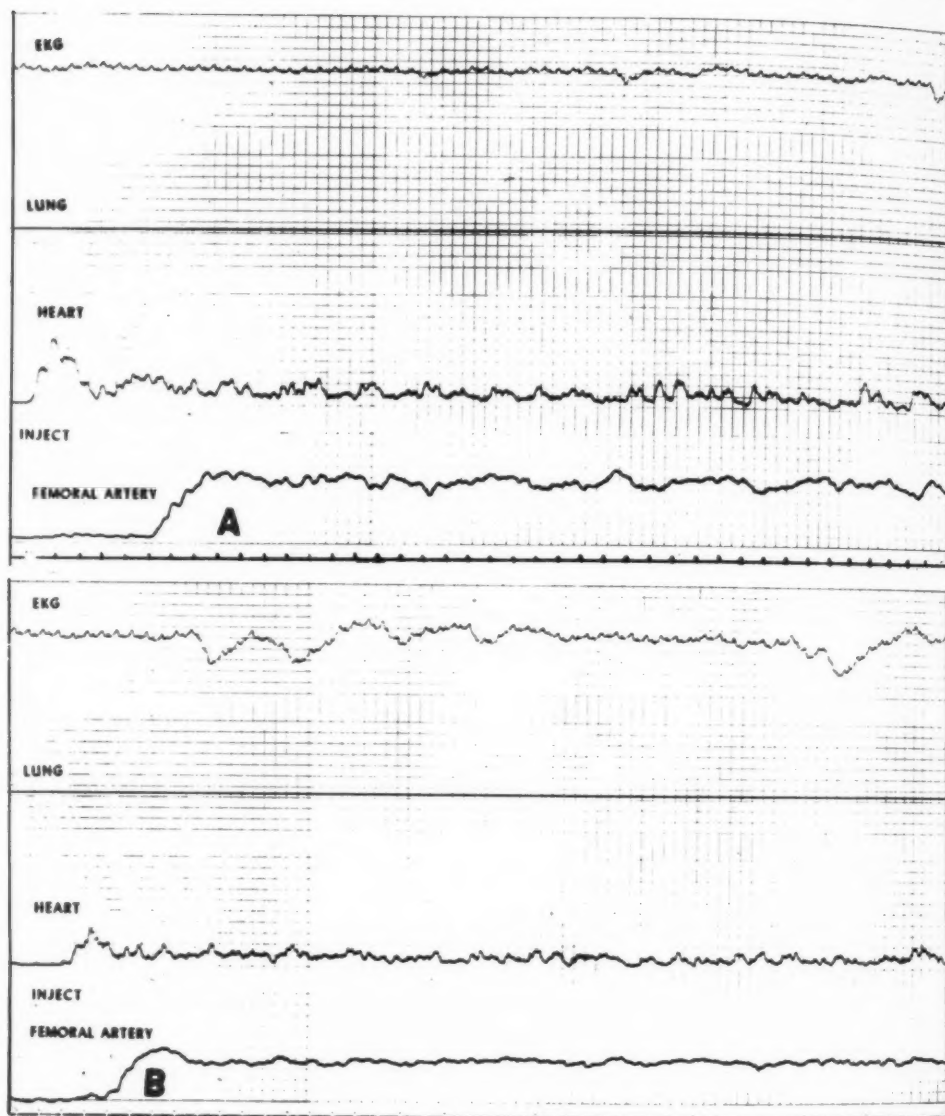


Fig. 7. Trilogy of Fallot. A. Right ventricle injection: Normal interval to femoral artery.  
B. Right atrial injection: Short interval to femoral artery.

large group may exhibit constant precordial curves, but we have not observed these in our limited experience.

In addition to detecting right-to-left shunts, the isotope-circulation method can also be used to exclude their presence where they may be suspected in cyanotic individuals. Two grossly cyanotic adults were

studied with several injections. Before the isotope studies were made, both patients were considered clinically to have right-to-left shunts. Heart-to-femoral-artery time was greatly prolonged in each case, however, rather than diminished, as would be expected with right-to-left shunt (Fig. 8). On the basis of these

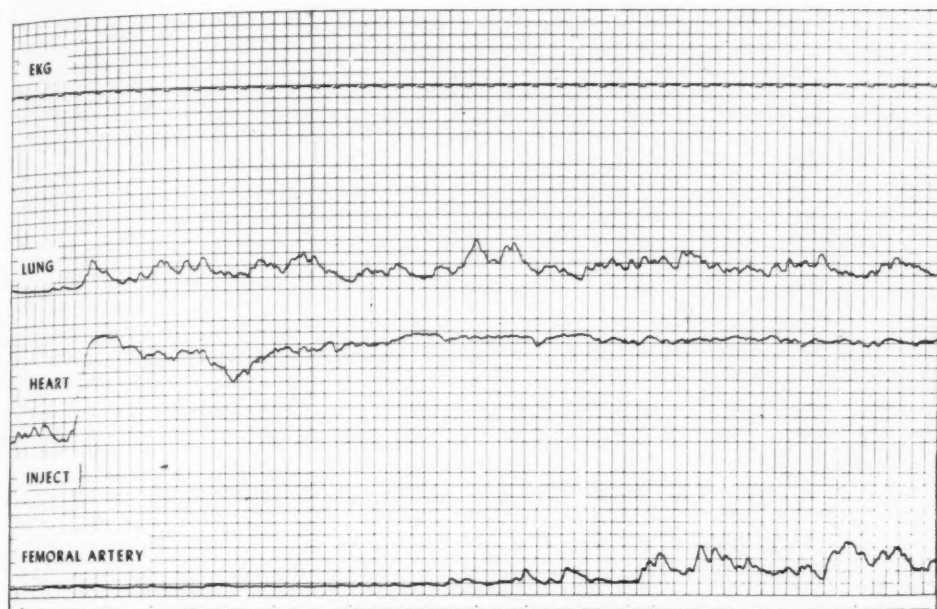


Fig. 8. Pulmonary obliterative arteritis: Delay in appearance peripherally with slow rise.

studies a diagnosis of obstructive pulmonary vascular disease was made. This was subsequently confirmed at necropsy.

Several patients with mitral valve disease have also been examined. In all a similar pattern, although of varying degree, has been observed. Appearance time at the peripheral artery is quite markedly delayed (up to twenty seconds), and a very gradual slope of increasing activity is observed by the peripheral counter. Patients in cardiac decompensation and those with particularly large hearts also exhibit a gradual rise in artery counts resembling tracings from patients with left-to-right shunts and mitral disease.

#### DISCUSSION

In any diagnostic procedure performed with radioisotopes, the amount of radiation delivered to the patient is an important factor. This is particularly true of infants and young children who are being exposed to fluoroscopy and angiocardiology. The retention of various forms of radioiodine in man is shown in Figure 9. It can be seen that the half-life of  $I^{131}$ -labeled

TABLE I: DOSE IN MILLIRADS FROM VARIOUS  $I^{131}$  TRACER SUBSTANCES\*  
(Administered dose = 1 microcurie per kg. body weight)

Material	Half Life	Total Dose	Beta Dose†	Gamma Dose	First Day
RISA	Four days	105	55	50	17
Methyl iodide	One day	26	13.7	12.6	13
Renografin	Six hours	6.5	3.4	3.1	6.1

\* Calculations based on formulas obtained from Hine and Brownell (12).

† Assumes uniform distribution throughout body.

Renografin is extremely short, averaging five hours in patients with normal kidneys. Dosage calculations based on a half-life of six hours, and a dose of 1 microcurie per kilogram of body weight, show a total dose of 6.5 millirads with 3.4 millirads of beta and 3.1 of gamma radiation. None of the  $I^{131}$  is concentrated in the thyroid. The dose delivered from a similar amount of human serum albumin is approximately sixteen times as great (Table I). Because of the promotion of rapid excretion, the tagging of a urographic contrast agent has been of great value in decreasing the dose.

This method was developed in an effort to simplify the detection and localization

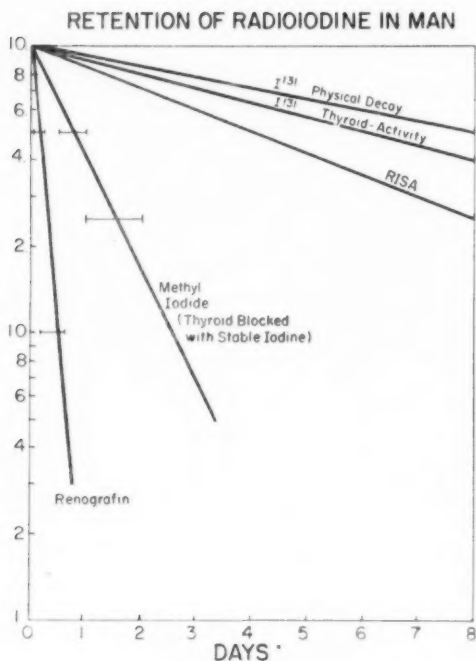


Fig. 9. Retention of radioiodine in man.

of right-to-left shunts. The entire study can be completed in a few minutes and can be done easily by a trained technician. Direct recording allows immediate interpretation of tracings.

Exact timing of the injection is unnecessary, since the interval from heart to peripheral artery is of interest, rather than from arm or catheter end, as with dye dilution. Electronic circuitry, which initially was bulky, complex, and rather undependable, has been condensed into a small, transistorized, compact, portable unit, which is very reliable.

As yet we have made no attempt to quantitate our studies, although standardization of the dose and recording apparatus should allow more precise measurements of dynamics. Several investigators have made determinations of this type and have calculated cardiac output. Goldring and his associates (4) employed radiocardiography with a single counter placed over the heart and studied patterns in normal subjects and in patients with congenital

heart disease. The Western Reserve group (5-7) has devised a method necessitating arterial puncture. Mack and his associates (8) placed a scintillation counter over the heart, as did Zacks (9), who recorded patterns of appearance and disappearance from the heart. Thode and his group (10) have studied circulation dynamics by means of inhalation radiocardiography, utilizing radioactive methyl iodide, and Case *et al.* (11) have utilized inhaled radioactive ethyl iodide to detect and locate left-to-right shunts.

#### SUMMARY

A method has been described for the detection of intra- and extracardiac shunts, by the use of trace amounts of radioiodine and external detectors. The method is very simple to use and requires little time. The need for femoral-artery puncture is obviated. Right-to-left shunts can be detected and accurately located. Typical patterns have been observed in mitral disease.

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#### SUMMARIO IN INTERLINGUA

##### Aspectos Clinic de Studios Isotopic del Circulation

Radioisotopos pote esser usate como instrumento physiologic in le detection e location de shunts intra- e extracardiac. Le technica del autores consiste in le injection de quantitates tracia de Renografin marcate con  $I^{131}$ , directemente in le bracio o via un catheter cardiac in varie cameras e vasos, sequite per le determination del tempores de re-apparition e del pertinente curvas per medio de collimate contadores de scintillation al extero del corpore. Le precise chronometrage del injection non es de importantia critic, proque il es le intervallo inter le corde e le arteria peripheric que in-

teressa nos e non un intervallo partiente ab bracio o extremitate del catheter.

Le instrumentos usate in iste studios esseva specialmente elaborate. Le circuiteria electronic—initialmente massive, complexe, e capriciose—esseva condensate in un micre, compacte, e portative unitate que es construite con transistores e functiona multo uniformemente.

Shunts ab le dextera verso le sinistra pote esser detegite e locate accuratemente. Patronos typic ha essite observate in morbo mitral. Le methodo es simple e non require multe tempore. Le requirimento de punctura femoro-arterial es obviate.





# Acute Mercury Vapor Poisoning

A Report of Four Cases with Radiographic and Pathologic Correlation<sup>1</sup>

CHING TSENG TENG, M.D., and JAMES C. BRENNAN, M.D.

ACUTE MERCURY poisoning is commonly caused by accidental ingestion of soluble mercurial compounds. The clinical manifestations are an accurate portrayal of the severe ulcerative and necrotizing inflammation of the entire gastrointestinal tract. The excretory organs, the central nervous system, and other internal organs are secondarily involved. More rarely, acute poisoning may result from the inhalation of mercury vapor. In this event, the respiratory epithelium, being the primary site of contact, bears the brunt of the injury, and respiratory symptoms dominate the clinical picture. The central nervous system, kidneys, liver, and gastrointestinal tract may also be affected, usually to a mild degree at most, through absorption in the respiratory tract.

Two papers reporting acute mercury vapor poisoning as a result of industrial mishaps (2, 5) and 2 reporting domestic accidents (1, 3) were found in a brief survey of the literature. The common features are (a) the inhalation of mercurial fumes caused by heating of metallic mercury and (b) the prominence of respiratory symptoms. Radiographic findings are included in the accounts of the domestic accidents. One of these patients was a four-month-old infant who succumbed to the intoxication in three days (1). The chest film (not published) showed (a) circumscribed opacities in both upper lung fields interpreted as atelectasis; (b) minor infiltration at right base; (c) diffuse compensatory emphysema; (d) left-sided pneumothorax. A postmortem examination was not performed. In the other patient, a twenty-nine-year-old man, the chest film showed "bilateral bronchopulmonary abnormalities probably indicative of aspiration and exudative type

bronchitis" (3). In this instance recovery ensued after ten days hospitalization. The radiographic evidence of chemical pneumonitis had completely resolved in fifteen days.

A family of four, a nineteen-year-old mother and her three children, thirty months, twenty months, and four months of age, suffering from acute mercury vapor poisoning, which ended fatally for all the children, has been observed in our hospital. The radiographic findings, not fully described in the case report published elsewhere (4), and their correlation with the postmortem findings are presented in this communication.

## CLINICAL HISTORY

*The History of the Tragedy:* A Negro family of four—a nineteen-year-old mother and her three children, thirty months, twenty months, and four months—lived in a two-room apartment. The family was apparently in good health before their exposure to mercury fumes on the night of Feb. 28, 1957. The father was away from home at the time.

The illness seized all four patients on the same night and was characterized by severe respiratory distress, cough, diarrhea, and mental depression. Before the diagnosis was even suspected, death claimed the first victim (Case I, W. D., twenty-month-old girl), thirty-six hours after the onset of symptoms, while the family was on the way to the hospital. A postmortem examination was performed. The mother and two children were admitted to the hospital with the provisional diagnosis of viral pneumonitis.

It was then learned that on the evening of Feb. 28 the mother had painted a gas heater with a mixture of mercury, turpentine, and aluminum paint and had kept the heater lighted throughout the night, while the family slept in their small bedroom with all windows tightly closed. When they were found by the grandmother the next morning, they had been exposed to the mercury vapor for sixteen hours.

Upon learning the story, the pediatrician made a visit to the home. His findings have been recorded (4). Suffice it to mention that about 300 to 350

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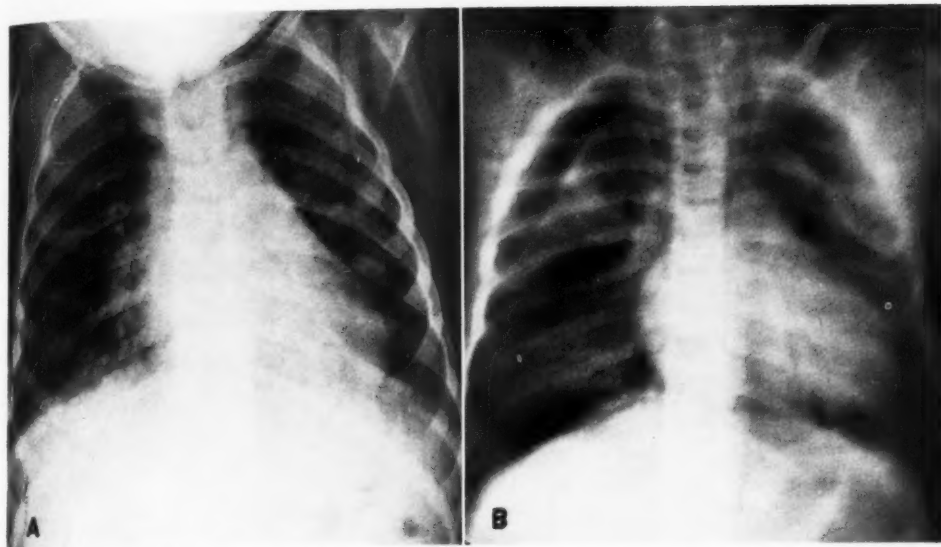


Fig. 1. Case II. Thirty-month-old boy. Acute mercury vapor poisoning ending fatally thirty-six hours after onset of symptoms.

A. Chest film on day of admission, March 2, 1957, showing marked diffuse emphysema, pulmonary edema more marked in the upper lung fields, and perihilar and infrahilar peribronchial infiltrations.

B. Chest film shortly before death on March 3, showing bilateral spontaneous pneumothorax, pneumomediastinum, and interstitial emphysema of the soft tissues of the neck. Pulmonary edema and emphysema prevented a greater degree of collapse of the lungs.

gm. of mercury had been used in the paint mixture.

**Clinical Features:** The symptomatology was similar in all 4 patients. The dominant feature was extreme air hunger with markedly increased respiratory rate, ranging from 40 to 80 per minute. Cough was present but not severe. Cyanosis was not conspicuous, as the patients were given constant oxygen inhalation. Fever was not high. Leukocytosis was variable but mild. Considerable tachycardia was present. Cerebral symptoms, such as lethargy and restlessness, were prominent and present in all. Diarrhea and abdominal cramps were relatively minor. Urinary symptoms were insignificant, although large quantities of mercury were demonstrated in the urine. Blood, urine, and spinal fluid cultures were negative.

**The Clinical Course:** All three children died from the intoxication. W. D. (Case I), as stated above, succumbed thirty-six hours after the onset of symptoms. L. D. (Case II) and I. D. (Case III) died on the third and the sixth day of illness, respectively. Only the mother, R. D. (Case IV), survived. She was dismissed from the hospital after twenty-eight days.

#### RADIOGRAPHIC FINDINGS

Serial examinations of the chest were obtained in Cases II, III, and IV. Many findings were strikingly similar in all cases, although the changes differed in severity

and varied in extent at different times (Figs. 1-3).

In all cases, the diaphragm was markedly depressed and presented a sloping contour, indicating a considerable degree of diffuse emphysema, suggesting bronchiolitis with bronchiolar obstruction. In the lung fields, areas of increased density were mingled with areas of increased lucency. The denser areas were ill defined. They varied in size, were not segmental in distribution, and showed no conspicuous vascular markings or air bronchographic pattern. They gave the impression of a structureless haze, more suggestive of pulmonary edema than of pneumonic consolidation.

Closer scrutiny revealed the presence of streaky and irregular, roughly circular areas of increased lucency, showing wide variation in size. They differed decidedly in appearance from an air bronchographic pattern. They were not large enough nor well enough defined to be pneumocysts. They proved to be due to interstitial emphysema.

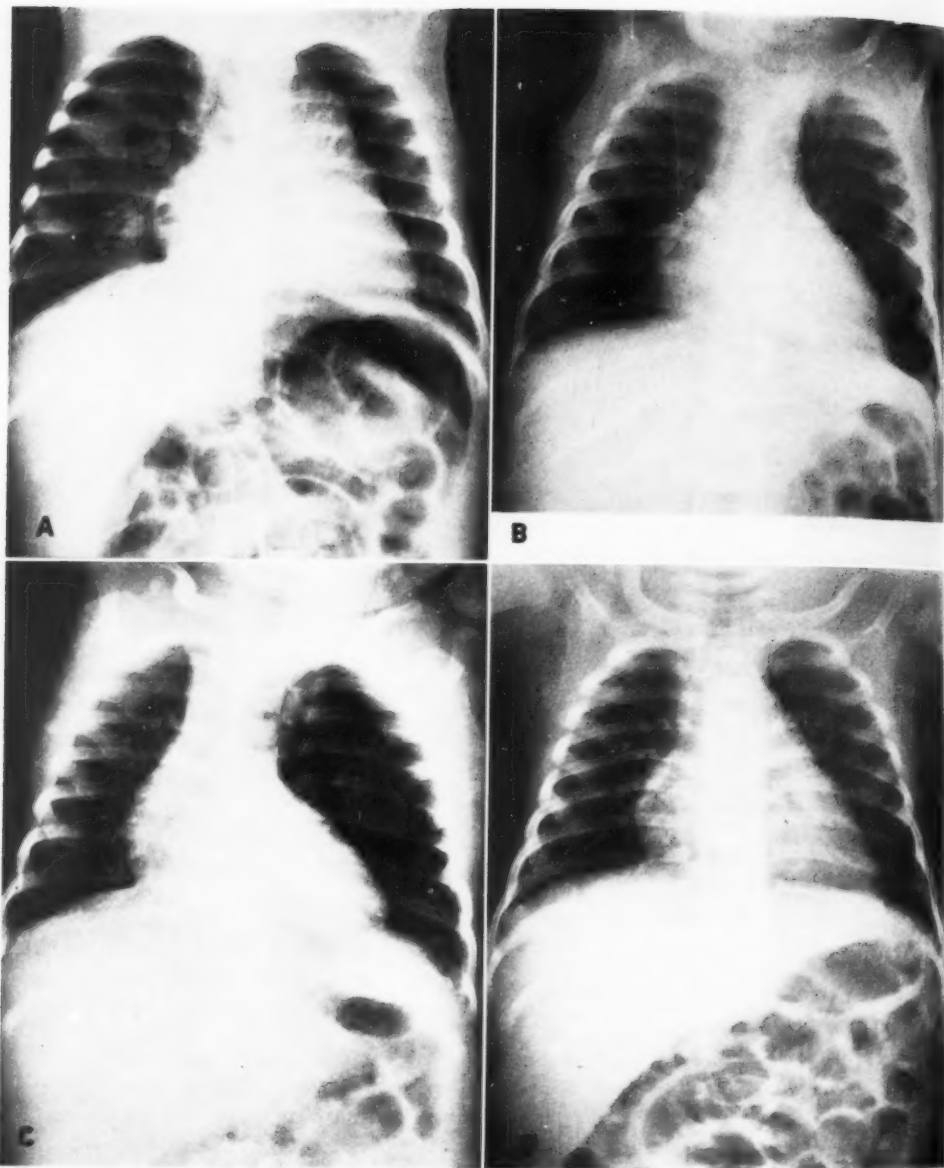


Fig. 2. Case III: Four-month-old female infant. Acute mercury vapor poisoning ending fatally four days after admission to hospital.

A. Chest film on day of admission March 2, 1957, showing bilateral diffuse alveolar and interstitial emphysema, right-sided spontaneous tension pneumothorax with air all around the right lung, and herniation of the pleural sac across the superior mediastinum. The relatively minor degree of collapse of the right lung and its hazy structureless appearance indicate loss of elasticity due to pulmonary edema as well as emphysema. There are also intralobar peribronchial infiltrations.

B. Chest film on March 4, showing spontaneous resorption of pneumothorax and persistence of other changes seen in A.

C. Chest film on March 5. Spontaneous pneumothorax in left chest. Again the degree of collapse of the left lung is not proportional to the degree of increased intrapleural tension as evidenced by the herniation of the pleural sac across the superior mediastinum to the right. The appearance of the left lung is that of marked emphysema. The presence of pulmonary edema could easily be masked by the emphysema and pneumothorax. The basal infiltration has increased.

D. Chest film on day of death, March 6, showing spontaneous resorption of pneumothorax and persistence of other changes.

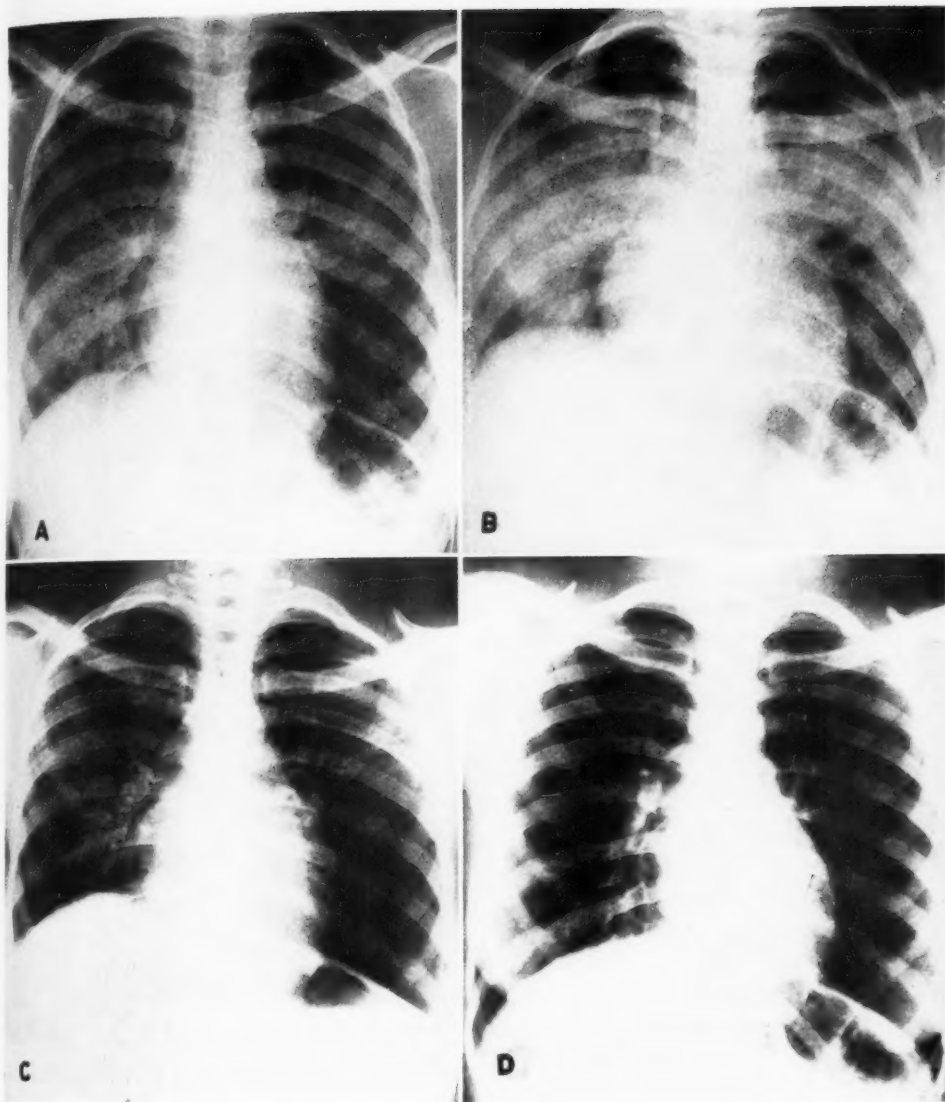


Fig. 3. Case IV. Nineteen-year-old mother, the only survivor of acute mercury vapor poisoning in a family of four.

A. Chest film on day of admission, March 2, 1957, showing large ill defined areas of increased density due to inflammatory pulmonary edema, more extensive in right than in left lung. Note also bilateral obstructive emphysema.

B. Chest film on March 3, showing pulmonary edema at its height. Apparent cardiac enlargement may be partly due to the antero posterior projection.

C. Chest film on March 13, showing resolution of pulmonary edema, with residual changes suggesting fibrosis. In the fatal cases, it is at this stage of resolution that hyaline membrane formation is a conspicuous feature microscopically. Note the persistence of emphysema, especially of the left lower lobe.

D. Chest film at last follow-up on April 26, 1957, almost two months after onset of illness. There is still an abnormal diaphragmatic silhouette, suggesting persistent bronchiolar obstruction.

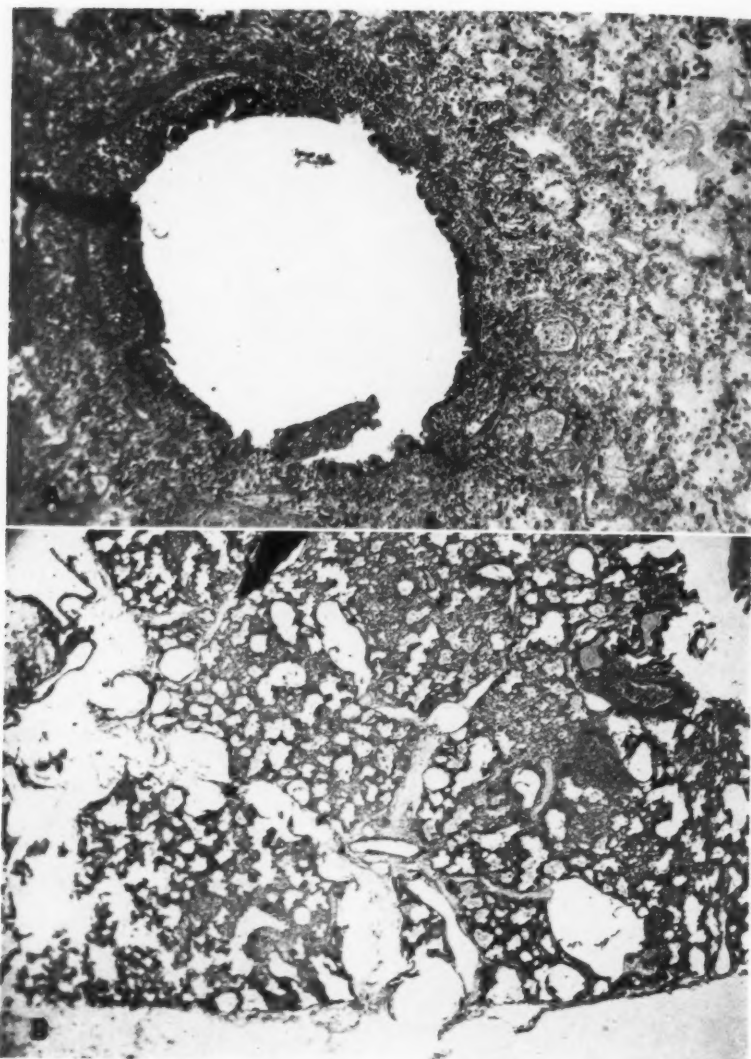


Fig. 4. A. Acute necrotizing bronchiolitis in Case I. There are focal necrosis, desquamation of mucosal epithelium, and early acute cellular infiltration of the bronchiolar wall.

B. Marked dissection of air along interstitial plane and rupture through pleura in Case III. Note occasional interstitial micropneumatocele.

In both Case II and Case III, there was spontaneous pneumothorax. In Case II, bilateral pneumothorax and pneumomediastinum occurred terminally (Fig. 1, B). In Case III, right-sided pneumothorax was observed at the time of admission (Fig. 2, A). It had re-absorbed spontaneously before pneumothorax occurred in the left chest three days later (Fig. 2, C).

In both cases free air was present in the interlobar fissures and in the mediastinal pleural spaces. In Case III there was herniation of the pleural sac across the superior mediastinum in both instances of pneumothorax (Fig. 2, A and C), yet the lung was relatively little collapsed. These findings further attest the loss of pulmonary elasticity due to the presence of



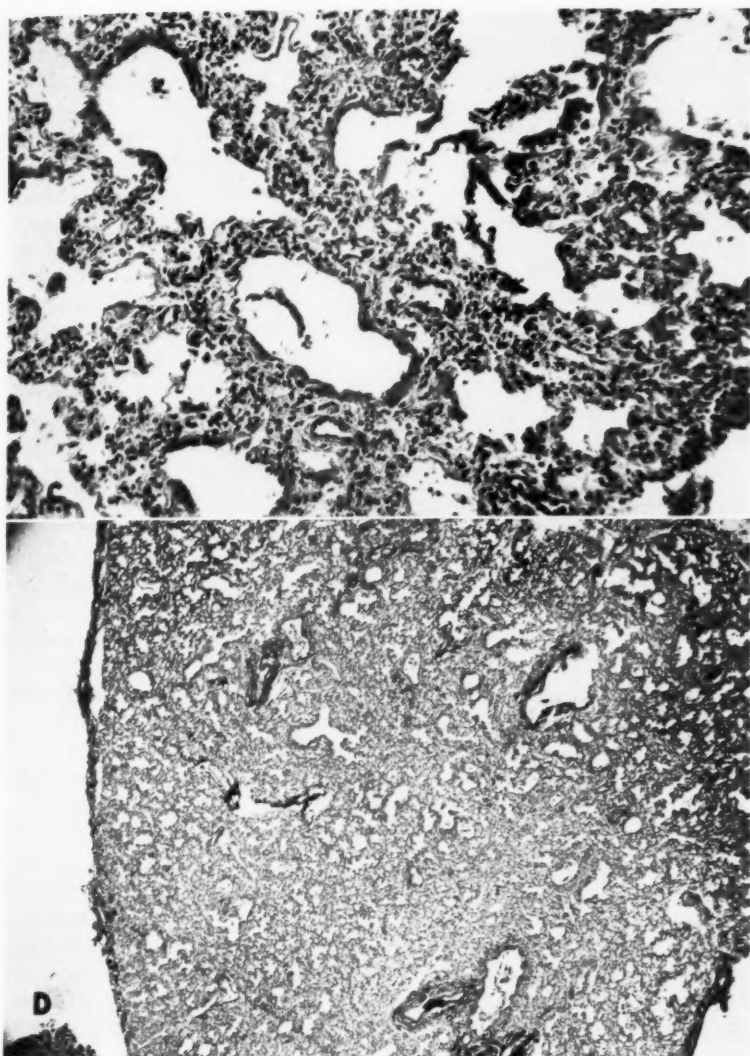


Fig. 4. C. Well formed "hyaline membrane" of alveolar ducts in Case II. Note only minimal infiltration of inflammatory cells of interstitial tissues.

D. Low-power photomicrograph demonstrating the "fixation" of the lung tissues in Case III in the stage of inflammatory cell infiltration of the interstitium.

inflammatory edema, as well as obstructive emphysema.

In the case of the mother, who survived, serial chest films showed the evolution of the inflammatory edema of the lungs until complete resolution (Fig. 3).

#### PATHOLOGIC FINDINGS

The findings at autopsy in the fatal

cases are described elsewhere (4). The lung changes can be closely correlated with the radiographic sequence. Their pathogenesis may be attributed to the two major reactions of the pulmonary tissues to an inhaled cytoplasm-coagulating agent:

1. *Acute exudative edema* appears as the initial inflammatory response in the lung to the inhalation of mercury vapor,

occurring in the alveolar spaces and the interstitial tissues. Some features of this inflammatory exudate might be elaborated upon. Because of its high protein content, the weight of the exudate in the lung might be expected to be greater than that of noninflammatory pulmonary edema. The exudate is more diffuse and tends to affect the upper lobes to a greater degree than the lower lobes, differing in this respect also from noninflammatory edema. Because the interstitial areas are involved in the exudate, there is more involvement of unit tissue in the lung. As a result of these factors, the increase in weight of the lung is relatively greater than in non-inflammatory edema.

2 *Acute necrotizing bronchiolitis:* The columnar cells lining the bronchiole and bronchus are slightly more resistant to external irritants than are the alveolar lining cells. The bronchiolar injury appears as a superficial erosion of the lining cells due to cytoplasmic coagulation by the inhaled mercury, causing cell death and desquamation (Fig. 4, A). The acute cellular reaction with inflammatory exudate appears to commence in the bronchioles, later extending along interstitial planes away from areas of erosion. The acute desquamation of the erosions, along with the intense injury to denuded bronchioles and bronchi, leads to mechanical blockage of bronchioles by excessive mucus secretion, desquamated epithelium, inflammatory exudate cells, and protein-rich edema fluid. This bronchiolar block appears sufficient to prevent egress of expired air, but without similar blockage of inspiration. The consequences are (a) dilatation of alveoli and alveolar ducts, (b) inspissation of retained exudative edema fluid in alveolar ducts and alveoli (Fig. 4, C), and (c) rupture of alveolar walls, resulting in interstitial emphysema, micropneumatocele formation, pneumothorax, and mediastinal emphysema that are seen radiographically and histologically in these cases (Fig. 4, B). It is worthwhile noting in passing that the lungs *do not* collapse significantly even when a considerable pneu-

mothorax may be present. Instead, the interstitial emphysema and the considerable exudative edema tend to maintain such tissue support as to present at autopsy an appearance of "normal size and shape" of all lobes of the lungs, even though the alveoli may be empty of air when examined histologically. The pneumothorax may be missed at autopsy when the "normal size" of the lungs seems to conflict with the presence of intrapleural air. With regard to the inspissation of the edematous exudate in the alveoli and alveolar ducts, it is apparent that the "hyaline membrane" appearance seems even more striking than in the lungs of infants with "hyaline membranes" dying after respiratory distress in the immediate neonatal period (Fig. 4, C).

If the patient survives the period of "air block" and interstitial emphysema, the "hyaline membrane" lesion becomes apparently the dominant histologic feature, associated with a considerable reduction in lung weight due to re-absorption of much of the edema fluid. At the same time increasing amounts of interstitial cellular exudates, largely mononuclear, but with polymorphs and occasionally eosinophils, may be seen in the vicinity of fragmented "hyaline membranes," where the latter lie in close contact with the tissues of the alveolar septa. This change may be correlated radiographically with the increasing reticulation in the interstitial planes of the lungs. Later still, the histologic picture reverts to one of interstitial pneumonitis predominantly, the infiltrating cells in the interstitial tissues being almost totally histiocytic in type (Fig. 4, D). In the later stages of this inflammatory reaction, hilar lymph node enlargement may be noted and may even tend to slow resolution of the interstitial pneumonitis by compression of hilar bronchi.

It only remains to state that a truly exudative pneumonia, even of a focal nature, does not appear to occur as a primary reaction to mercury inhalation, but rather follows secondary infection of tissues so injured. The areas of "consoli-

dation" or of "increased density" in the radiograph appear to represent lung lobules that are full of interstitial and alveolar protein-rich edema fluid, usually alternating with and compressed by areas of alveolar and alveolar duct dilatation or "focal emphysema."

#### CORRELATION BETWEEN PATHOLOGIC AND RADIOGRAPHIC FINDINGS

The radiographic findings as shown in the serial examinations correlate well with the sequence of events that may be reconstructed from the gross and microscopic appearance of the lungs at postmortem examination of our three fatal cases.

#### SUMMARY

Four cases of acute mercury vapor poisoning in a mother and three children, thirty, twenty, and four months of age, are reported. All three children succumbed to the intoxication; only the mother survived. The major pathologic changes in these cases are found in the lungs, and death is attributable to loss of respiratory function as a result of severe injury of the pulmonary tissues.

#### SUMMARIO IN INTERLINGUA

##### Invenenamento Acute per Vapores de Mercurio: Reporto de Quatro Casos, con Correlation Radiographic e Pathologic

Es reportate quatro casos de acute invenenamento per vapores de mercurio. Le patientes esseva un matre e su tres infantes de etates de trenta, vinti, e quatro menses. Solmente le matre superviveva. Le major alterationes pathologic in iste casos se trova in le pulmones, e le morte es attribuibile al perdita de function respiratori in consequentia de sever injurias in le histos pulmonar.

Pathologicamente le lesiones primari

Pathologically the primary lesions are (1) acute exudative pulmonary edema and (2) acute necrotizing bronchiolitis. Secondary to these primary reactions are (1) bronchiolar obstruction of the check-valve type, (2) alveolar and interstitial emphysema, (3) tension pneumothorax, (4) hyaline membrane formation, (5) secondary bacterial pneumonitis, and (6) different phases of resolution.

All of these changes are demonstrated in serial chest films.

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es (1) acute exsudative edema pulmonar e (2) acute bronchiolitis necrotisante. Iste reacciones primari es sequite secundariamente per (1) obstruction bronchiolar del type valvula de retention, (2) emphysema alveolar e interstitial, (3) pneumothorace tensional, (4) formation de membrana hyalin, (5) pneumonitis bacterial secundari, e (6) phases diferente de resolution.

Omne iste alterationes es demonstrate in radiogrammas thoracic in serie.

## Unilateral Pulmonary "Emphysema"<sup>1</sup>

ISADORE KATZ, M.D., and STEPHEN WAGNER, M.D.<sup>2</sup>

**I**NCREASED RADIOLUCENCY of one lung associated with decreased prominence of its hilar and pulmonary vascular markings is observed most commonly in obstructive emphysema due to occlusion of a main or lobar bronchus by a mass or foreign body and in compensatory emphysema following collapse of a pulmonary lobe or segment. Recently, however, there have appeared several reports describing a condition in which the roentgen findings simulate obstructive or compensatory emphysema but which proves on further roentgen examination to be neither. The first comprehensive analysis of a group of such patients was made by Macleod, who reported 9 cases under the title *Abnormal Transradiancy of One Lung* (2). Later Dornhorst, Heaf, and Semple (1), designating the process as "unilateral emphysema," described 4 additional examples and reported follow-up studies on 5 of Macleod's original cases. Neither of these reports identifies the disease as one of the recognized forms of pulmonary emphysema. Actually the first case, in a boy of six years, was reported by Swyer and James, who entitled their paper *A Case of Unilateral Pulmonary Emphysema* but were careful to point out the clinical and roentgen features distinguishing the process from both compensatory and obstructive emphysema (6). Even though it may eventually prove to be incorrect, it seems preferable to designate the lesion as "emphysema" rather than as "abnormal transradiancy," which is a purely roentgenographic description.

The cardinal point of differentiation of unilateral "emphysema" from other forms of airway obstruction is the absence of major bronchial occlusion demonstrable by bronchography. In most of the patients movement of the mediastinum is toward

the abnormal lung on inspiration, the opposite of what takes place in obstructive emphysema.

The present paper describes a case which is representative of those previously reported.

### CASE REPORT

A 38-year-old male, a machinist, was referred for study in July 1955 because of an abnormal chest roentgenogram. He was asymptomatic except for occasional dry cough and mild exertional dyspnea. He gave a history of a severe respiratory illness in childhood which was diagnosed as "pneumonia" and treated at home, with no apparent sequelae. There were infrequent "colds" which cleared readily.

The left hemithorax was hyperresonant and the breath sounds were decreased. Cardiovascular examination was normal.

Roentgen study showed the left hemithorax to be slightly smaller and much more radiolucent than the right. There was a striking decrease in the vascular markings, with a corresponding decrease in the size of the hilar shadow on the left side. The right lung showed a marked increase in prominence of the vascular markings. There was minimal displacement of the mediastinal structures to the left side. The left leaf of the diaphragm was slightly flattened (Figs 1 and 2).

Films of the thorax made in 1943, when the patient was twenty-five years of age, indicated that the roentgen appearance of the left lung was the same twelve years earlier. He was re-examined in 1958 and again there was no appreciable change in the appearance of the abnormal lung.

Fluoroscopy showed the mediastinum in the midline during quiet respiration. With deliberate deep inspiration it moved toward the abnormal side. This phenomenon was best demonstrated when the speed and force of the inspiratory effort were increased, as with sniffing. With expiration or with coughing, the mediastinal shift was away from the abnormal lung, which then showed a marked increase in volume and enhanced translucency. With forced maximum expiration, the mediastinal structures shifted markedly toward the normal lung, the right leaf of the diaphragm ascended sharply, and the trachea became displaced far to the right. The left leaf of the diaphragm rose only slightly during this effort at forced expiration (Fig. 3).

Bronchographic study showed the right bronchial

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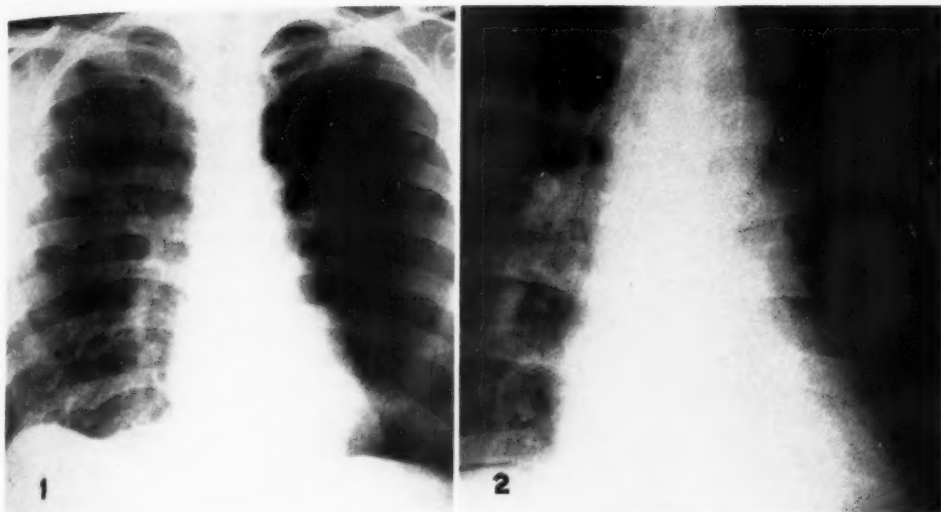


Fig. 1. Inspiratory roentgenogram of thorax showing uniform marked increase in radiolucency of the left lung. The left hemithorax is slightly smaller than the right. The mediastinal structures are displaced minimally toward the left. This is best demonstrated during the fluoroscopic examination. There is marked decrease in lung markings on the left. The hilar shadow and pulmonary vessels are virtually absent as compared with the right side, where there is a luxuriant vascular supply. The left leaf of the diaphragm is flattened. The width of the rib interspaces on each side is the same.

Fig. 2. Close-up view of Fig. 1, showing in detail the contrasting size of the vascular and hilar structures.

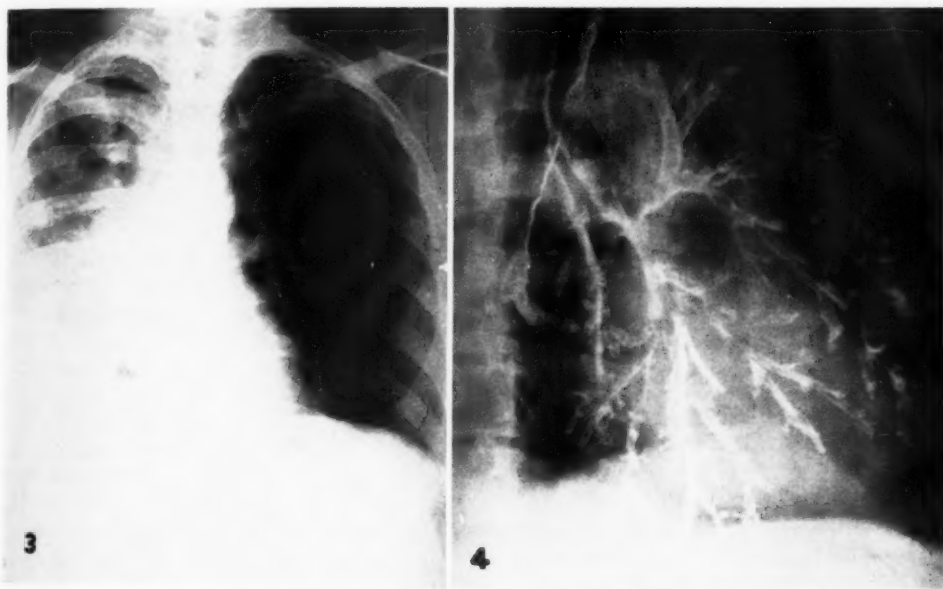


Fig. 3. Roentgenogram of the thorax at the end of forced expiration showing "hyperinflation" of the abnormal lung and marked shift of the mediastinum to the right. The findings during this phase of the study simulate the check-valve type of (obstructive) emphysema such as is found with occlusion of a major bronchus due to tumor, foreign body, etc.

Fig. 4. Close-up (left oblique) view of abnormal bronchial tree of the left lung. All of the major bronchi are patent and of normal caliber. Note the uniformity and totality of distribution of the small, bulbous, bud-like sacs. The bronchi show only slight tendency to taper. The right bronchial tree (not shown) was normal.



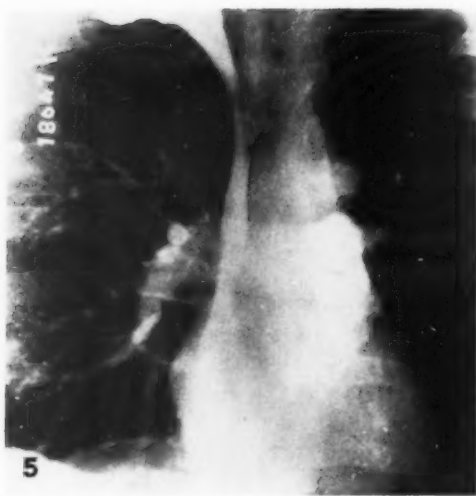


Fig. 5. Angiocardiogram at two seconds after injection, showing marked hypervascularity of the right lung with only a few opacified thread-like vessels on the left. Note the relationship of the main pulmonary artery to its right branch, which emerges at a right angle. The branching root of the left pulmonary artery may also be seen at a slightly higher level than the right. There is no smooth, sharply arcing sweep of a single vessel as in congenital absence of a main branch of the pulmonary artery.

tree to be normal. The left main bronchus and its primary segmental branches were fully developed and equal in size to those of the right lung. No bronchial obstruction was present. The subsegmental bronchi showed only a slight tendency to taper, remained tubular, and terminated abruptly in blind saccular expansions or in small bulbous, bud-like processes. There was no filling of the peripheral bronchi. The peculiar terminal "buds" were fairly uniform in size and distribution throughout the entire bronchial tree (Fig. 4).

Angiocardiography revealed normal filling of the right heart chambers and main pulmonary artery. The right pulmonary artery and its primary divisions were enlarged, and a luxuriant vasculature appeared to obliterate almost entirely the air-containing portions of the lung (Fig. 5). The left lung was virtually avascular. The injected contrast material produced only a barely perceptible increase in the density of the few slender vessels branching from the left hilar region (Fig. 5). There was no demonstration of a bronchial arterial system.

Bronchoscopic examination disclosed no obstruction or other abnormality in the left main bronchus and its subdivisions.

Pulmonary function and bronchspirometry studies (Aug. 11, 1955) showed maximum breathing capacity and timed vital capacity to be moderately diminished. Bronchspirometry readings revealed greatly diminished tidal air on the left, with the left lung contributing only 10 per cent of the total tidal

volume. The complementary air (inspiratory reserve) and supplementary air (expiratory reserve) were likewise decreased, but to a lesser degree. The findings were interpreted as those of severe ventilatory obstruction of the left lung. The right lung was found to be normal. Minute oxygen consumption was greatly diminished on the left, showing a value of only 13 per cent.

#### DISCUSSION

**Clinical Features:** The previously reported cases, with one exception, were in adults, usually male. The histories often include childhood respiratory illnesses. The time of onset of symptoms is usually not noticed by the patients. The outstanding complaint is of mild to severe shortness of breath, usually following mild exertion. This develops slowly over a period of several years and may be aggravated by acute upper respiratory infections. Cough is occasionally present. A few patients are asymptomatic. The chief physical findings are decreased thoracic excursion, hyperresonance, and diminished breath sounds over the affected lung (1, 2).

**Roentgen Findings:** The characteristic roentgen features are unilaterally decreased prominence of the pulmonary vascular shadows and a corresponding decrease in size of the hilar shadow as contrasted with that of the opposite lung. In approximately 50 per cent of cases the mediastinum is displaced toward the affected side on inspiration. Expiratory films accentuate the radiolucency of the abnormal lung, while the normal side becomes less radiolucent as the mediastinum shifts away from the affected lung, moving either back to the midline from its position on the abnormal side or over into the normal lung field if originally in central position. The diaphragm on the affected side rises only slightly on expiration. In the remaining cases the mediastinum shifts away from the affected side on inspiration. The roentgen appearance of the lungs remains unchanged over the years (1, 2). In our own case films over a period of fifteen years showed no change.

**Bronchographic Findings:** Bronchography reveals complete patency of the bron-

chial system of the abnormal lung. No gross intra- or extrabronchial obstructive mechanism is found in the major or segmental bronchi, and their spatial distribution within the lung is usually normal.

No uniform pattern of abnormality appears to have been found in the bronchographic studies recorded. Among the defects noted are failure of peripheral bronchial filling (6), demonstration of "cystic loculi" (2), and the peculiar bud-like sacs noted in our patient. These are probably nonspecific changes common to a variety of lung diseases (4).

*Physiologic Studies:* The manner in which the abnormal lung functions mechanically was demonstrated by Macleod, who measured the pleural pressure during artificial pneumothorax in one patient and found a decrease in the elastic recoil of the lung (2). Similarly bronchspirometric studies in two other patients showed marked increase in resistance to inflation and retardation in the speed of deflation, while compliance studies indicated distinct impairment of distensibility. These changes in turn are thought to be responsible for a gross increase in airway resistance. With the impaired ventilation there is decreased blood flow, which in turn results in diminished oxygen consumption. The values recorded in our studies of pulmonary function are in agreement with those found in two previous cases (1).

It is easy to understand the peculiar movements of the mediastinum when one considers the interplay of lung volumes and pressures between a normal lung and one which inflates and deflates at a relatively much slower rate.

*Pathological Studies:* Lung specimen studies from only two patients have thus far been reported. In one the anatomic findings were reported as "cystic disease, acute and chronic bronchitis, and emphysema." The pulmonary artery was found to be of normal size despite its apparent decreased caliber as seen on plain films and during angiocardiographic examination (6). In the second patient there was chronic bronchitis with thinned, easily compres-

sible bronchial cartilages and pulmonary vessels which were smaller than normal (1). The nature of the basic pathologic process and the manner in which it produces or results in impaired lung function therefore remain unknown. One theory is that pulmonary infections during infancy or childhood may impair the growth of the lung. It is known that pulmonary growth continues after birth for as much or more than seven years by the addition of new lobules, rather than merely by an increase in size of the existing lobules (2, 4).

*Differential Diagnosis:* The conditions which most commonly simulate the entity we are describing are the obstructive and compensatory types of emphysema. These, however, may be differentiated readily by bronchography, which will demonstrate the affected portion of the bronchial tree. We have been able to find only one other lesion in which the plain film and fluoroscopic findings were virtually identical with those observed in our patient. This was a congenital pulmonary malformation which proved to be agenesis of the left lower lobe and stenosis of the left main bronchus (5). Here too, however, differentiation was simple, since the bronchial malformations were evident on the bronchographic study performed prior to surgical exploration of the thorax.

Even though congenital absence of one of the main pulmonary arteries produces unilaterally increased pulmonary radiolucency, there are other findings in the chest roentgenogram which distinguish this lesion. These include considerable reduction in the size of the affected lung and herniation of the normal lung anteriorly into the abnormal lung field. Nor is there any evidence of the peculiar shift of the mediastinum toward the abnormal lung or of expiratory obstruction on the affected side as in the condition we are describing. Finally, in unilateral "emphysema" angiocardigraphy actually reveals the presence of a right or left pulmonary artery root on the involved side (Fig. 5). In congenital absence of this vessel, there is a single smooth uninterrupted vascular arc, bending

sharply either to the right or left (3, 7).

*Clinical Course:* In all but one of the reported patients with unilateral "emphysema" the clinical course has been entirely benign. In our own patient the clinical and roentgenologic findings have remained stationary for at least the past fifteen years, which represent only the period covered by roentgen examinations of the thorax. Indeed, the condition has probably been present in this man for a much longer period, probably since infancy or childhood. There appears to be no particular increase in susceptibility of these abnormal lungs to infection.

#### SUMMARY

An additional case of a unique pulmonary disease with distinctive clinical and radiologic features but undetermined etiology is reported under the title of "unilateral pulmonary 'emphysema.'"

Pulmonary function and bronchspirometric studies in this patient revealed markedly reduced ventilation and decreased oxygen consumption by the abnormal lung. The values for these functions are in agreement with those found in previously reported cases and are consistent with ventilatory obstruction.

#### SUMMARIO IN INTERLINGUA

##### Emphysema Pulmonar Unilateral

Sub le designation de "emphysema" pulmonar unilateral, un caso additional es reportate de un unic morbo pulmonar que ha distinctive aspectos clinic e radiologic sed nulle etiologia determinate.

Studios de function pulmonar e studios bronchspirometric revelava in iste patiente un marcatamente reduce ventilation e un diminuite consumption de oxygeno per le pulmon anormal.

Le characteristics roentgenographic del condition es un unilateralmente reduce prominentia del umbras pulmo-vascular e un reduction correspondente del dimensiones del umbra hilar in comparison con le situation in le pulmon heterolateral.

The abnormal movements of the mediastinum and the increased airway resistance are believed to be a reflection of decreased pulmonary elastic recoil and distensibility.

The clinical course is almost invariably benign.

The condition should be differentiated primarily from obstructive and compensatory forms of pulmonary emphysema and congenital absence of a main branch of the pulmonary artery.

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In approximativemente 50 pro cento del casos le mediastino es displaciate verso le latere afficite durante le inspiration, sequite per un transition al altere latere durante le expiration.

Es opiniate que le anormalitates del movimento del mediastino e le augmento del resistentia in le vias aeree es un reflexion del reduce resalto elastic e del reduce distensibilitate del pulmon.

Le curso clinic es quasi invariabilmente de natura benigne. Le condition deberea esser differentiate primariamente ab formas obstructive e compensatori de emphysema pulmonar e ab absentia congenite del branca major del arteria pulmonar.

# Chronic Fibrous Mediastinitis Due to *Histoplasma Capsulatum* (Histoplasmal Mediastinitis)

Report of Three Cases with Different Presenting Symptoms<sup>1</sup>

COL. GEORGE F. LULL, JR., M.C.,<sup>2</sup> and MAJ. DEAN F. WINN, JR., M.C.<sup>3</sup>

RECENT EXPERIENCES reported by Salyer *et al.* (1), Gillespie (2), and Miller and his associates (3) indicate a new approach to the problem of chronic fibrous mediastinitis, which is of importance as one of the major causes of superior vena caval obstruction. Radiologists must be aware of this new concept, for they are in an excellent position to suggest the correct diagnosis.

Each of the three cases of mediastinitis recorded below presented in a different fashion, but in all *Histoplasma capsulatum* was identified in the surgical specimen removed at thoracotomy. Radiographs of the chest made prior to onset of symptoms are available in each case. In 2 cases pathologic changes were obvious. In the third, the changes were so slight as to be seen only in retrospect. The records do not indicate why they were not investigated. The first patient presented with a chronic cough and exertional dyspnea; the second with superior vena caval obstruction; the third with recurrent hemoptysis associated with sore throat. The course in each case was characterized by chronicity, and the initial symptoms were manifestations of secondary changes rather than being due primarily to the infectious process. Several problems in differential diagnosis were encountered, in that lymphoma, sarcoid, bronchial adenoma, and several other conditions were suggested by the roentgen changes.

## CASE REPORTS

**CASE I:** A white male, aged 26 years, was first hospitalized in November 1953, with exertional dyspnea, wheezing, and productive cough, and a history of frequent respiratory infections beginning in 1951. A 4 x 5-in. film in 1952 showed changes

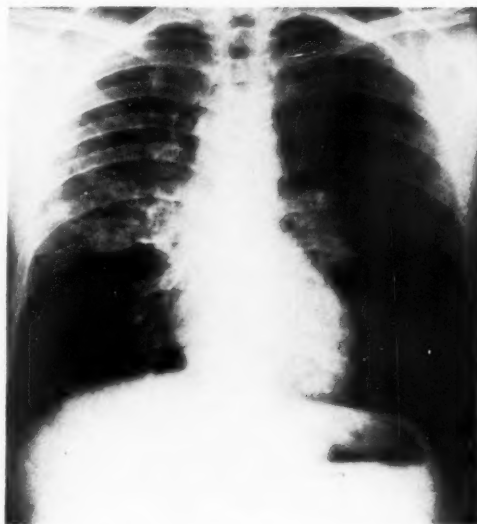


Fig. 1. Case I. Postero-anterior chest film at time of first hospitalization. Bilateral hilar adenopathy, infiltration of right upper and middle lobes, and widening of mediastinum above right hilus.

in the right lung and hili which had been overlooked. The admission film (Fig. 1) demonstrated hilar adenopathy, more marked on the left; linear and nodular infiltration in the right upper and middle lobes; and suggestive widening of the mediastinum above the right hilus.

The patient was transferred to this hospital in April 1954, with a diagnosis of lymphoma. His complaints were exertional dyspnea and chronic cough. The histoplasmin 1:1000 skin reaction was 3+; coccidioidin and P.P.D. #1 tests were negative; P.P.D. #2, 2+. Complement-fixation for histoplasmosis was positive in 1:16 titer; for blastomycosis and coccidioidomycosis negative. Repeated cultures were negative for *H. capsulatum* and *M. tuberculosis*. Bronchoscopy revealed hyperemia of the right main bronchial mucosa.

Chest films showed progressive parenchymal fibrotic changes, hilar adenopathy, suggestive mediastinal widening, and elevation of the right leaf of the diaphragm. At thoracotomy for biopsy, June 1954, there were found in the right lung disseminated

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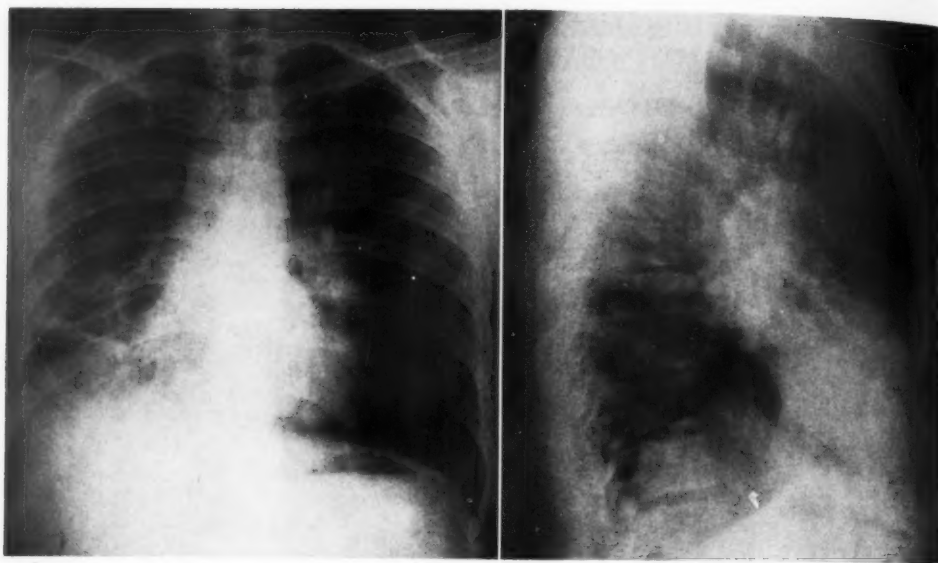


Fig. 2. Case I. Postero-anterior and lateral views nearly five years after Fig. 1 (June 1958), showing progression of the disease. Hilar adenopathy persists. There are extensive atelectasis and scarring in the right middle lobe. Smaller segmental scars are seen in the left upper lobe. Note residual fibrosis in right upper lobe.

TABLE I: SEROLOGIC RESULTS IN THREE CASES OF HISTOPLASMAL MEDIASTITIS

A. Case 1	3-21-58	4-23-58	5-22-58	6-17-58
Histoplasmosis				
YP Antigen	0	0	0	0
MF Antigen	1:16	1:8	1:8	1:16
Colloidin Agglut.	0	0	0	0
Blastomycosis	0	0	0	0
Coccidioidomycosis	0	0	0	0
B. Case 2	4-11-57	6-18-57	9-3-57	10-9-57
Histoplasmosis				
YP Antigen	1:16	1:8	1:16	1:32
MF Antigen	1:128	1:16	0	1:8
Colloidin Agglut.	0	0	Equiv.	Equiv.
Blastomycosis	1:8	0	0	0
Coccidioidomycosis	0	0	0	0
C. Case 3	5-28-57	6-26-57	8-20-57	9-24-57
Histoplasmosis				
YP Antigen	0	0	0	0
MF Antigen	1:64	1:64	1:64	1:64
Colloidin Agglut.	0	0	0	0
Blastomycosis	0	1:8	1:8	1:8
Coccidioidomycosis	0	0	0	0

nodules from 2 to 15 mm. in diameter, enlarged, boggy, friable nodes, and a stony-hard fibrotic mass encasing the mediastinal structures. Tissue sections showed chronic fibrous mediastinitis, granulomatous nodules containing *H. capsulatum*, and reactive hyperplasia of the lymph nodes. The patient was discharged with only minimal symptoms.

Small segmental densities were first noted in the left lung in 1956. In early 1958 respiratory infection, cough, and massive hemoptysis developed. Consolidation and atelectasis of the right middle lobe were demonstrated radiologically. Dyspnea

had increased. A bleeding point in the bronchus intermedius was cauterized to control hemoptysis. The histoplasmin skin reaction was now 4+. The serologic studies are recorded in Table I. Chronic endobronchial disease and stenosis of the right intermediate bronchus were observed on repeated bronchoscopies. Bronchial aspirations were negative for tumor cells. No acid-fast organisms were discovered by smear or culture. There was no response to therapy.

In June 1958, respiratory infection again developed, with tightness of the chest, increased



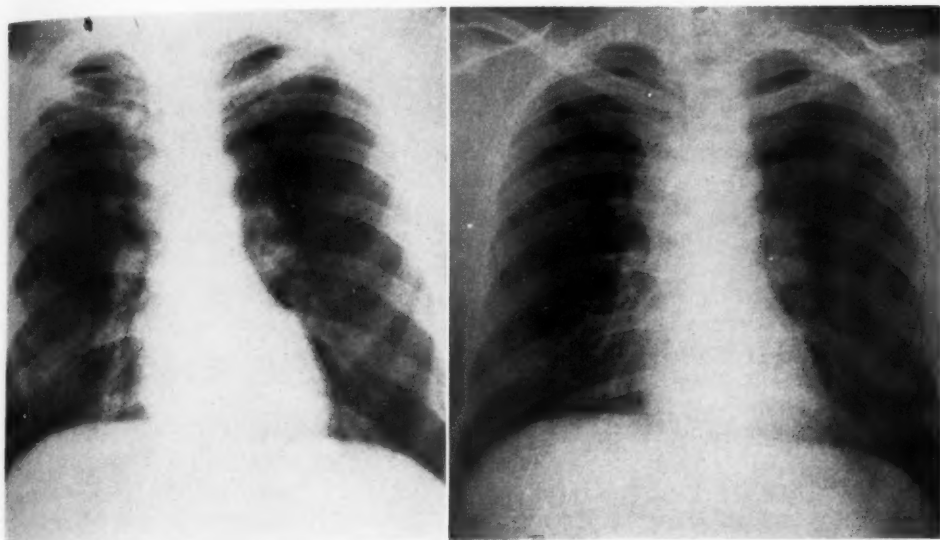


Fig. 3. Case II. A (left). Postero-anterior chest film in December 1955. Definite widening of mediastinum is apparent in this film made one year prior to onset of symptoms.  
B (right). Postero-anterior chest film in March 1957. This examination demonstrates extension of mediastinal widening in a superior direction.

dyspnea, and productive cough. There was an increase in the atelectasis of the right middle lobe (Fig. 2). The width of the mediastinum was unchanged, but superior extension of the process was noted. Experience with other cases of mediastinitis presenting on the right led to a prediction of superior vena caval obstruction. The attending physician reports that signs of such obstruction are developing very slowly.

A review of the films from 1953 to 1958 shows that there has been intermittent and recurrent atelectasis of segments of the right middle lobe, with recurrent secondary infection and progressive scarring.

CASE II: A white male, aged 26 years, first complained, in December 1956, of malaise, a 10-pound weight loss, and a sensation of pressure in the head on exertion. He was admitted to the hospital in March 1957 with obvious superior vena caval obstruction and moderately enlarged cervical and axillary lymph nodes.

A photofluorogram (Fig. 3, A) one year prior to onset of symptoms disclosed a mass projecting to the right of the sternum, but its superior extension was less marked than on a film obtained in March 1957 (Fig. 3, B). Fluoroscopy and films showed the mass to be predominantly right-sided, with no esophageal or tracheal compression. Blood, urine, and liver function studies were normal. Histoplasmin 1:100 gave a 2+ reaction; reactions to coccidioidin and P.P.D. #2 were negative. Scalene and axillary lymph node biopsies were reported as showing reactive hyperplasia. Results of serologic studies (Table I) were not available for guidance in

treatment. The provisional diagnosis was lymphoma.

Thoracotomy on March 27, 1957, because of progressive obstruction, and to obtain tissue for diagnosis, showed no palpable disease in the lung



Fig. 4. Case II. Venogram demonstrating recurrence of superior vena caval obstruction.

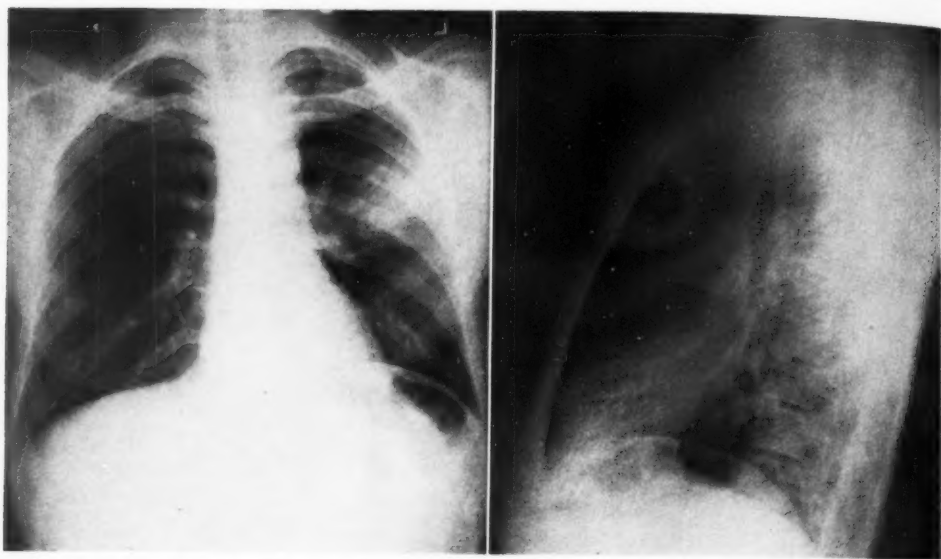


Fig. 5. Case III. Postero-anterior and lateral films. Density in anterior segment of left upper lobe and minimal degree of mediastinal widening.

parenchyma. A fixed, hard, encapsulated mass, 7.5 cm. in diameter, involved the superior vena cava, azygos and innominate veins, trachea, and right bronchus. Below the thickened, scarred capsule was a caseating fibrous mass, grossly a granuloma. Frozen sections showed no evidence of neoplasm. An arterial homograft was used to reconstruct the obliterated superior vena cava and right innominate vein. Fixed sections showed dense collagenous connective tissue heavily infiltrated with lymphocytes. Aggregates of *H. capsulatum* were identified in the caseating granuloma. Stains for acid-fast organisms were negative.

Symptoms of superior vena caval obstruction disappeared following surgery. Evidence of reocclusion was noted in five months, but the signs and symptoms were less severe than originally, indicating that there had been some development of collateral circulation. This was confirmed by venography (Fig. 4).

The patient was last seen in August 1958 and stated that he was comfortable on restricted activity. The mediastinal mass was unchanged at this time.

**CASE III:** A Negro male, aged 27 years, was hospitalized in May 1956 for sore throat and blood-tinged sputum of eighteen hours duration. A similar brief episode had occurred in 1952. Physical examination was normal. Films of the chest showed a rounded, homogeneous shadow 4 cm. in diameter, with ill-defined borders, in the left upper lobe, in the anterior segment distribution. This was interpreted as acute pneumonitis, and complete resolution was observed in ten days. There was no leukocytosis and the sedimentation rate was normal.

Positive skin reactions were obtained with P.P.D. #2 and histoplasmin 1:100. Bronchoscopic findings were normal. Esophagoscopy revealed extensive vascularity but no other abnormal finding. Repeated smears and cultures of the sputum and of bronchial washings were negative for *M. tuberculosis*.

On re-hospitalization March 1, 1957, because of hemoptysis lasting twenty-four hours, physical findings were again normal. Chest roentgenograms (Fig. 5) showed a spherical, soft area of infiltration in the same location as before, with some increase in markings in the lingula. Resolution was again complete in ten days. Bronchoscopy revealed only a small blood streak in the left upper lobe bronchus. Left scalene node biopsy was reported as showing reactive hyperplasia. Results of serologic studies are recorded in Table I.

One observer, in 1956, suggested the presence of a mass in the superior mediastinum, but further investigation was not accomplished. A film review in March 1957 demonstrated slight but definite extension of the upper mediastinal shadow to the left. Recurrent hemoptysis and parenchymal infiltration were postulated as secondary to a segmental bronchus lesion. Thoracotomy was advised.

A stony-hard, fibrous mass encased the bronchus to the lingula, pulmonary artery, and the great vessels from the arch of the aorta. The fixed sections showed dense, swollen, avascular collagenous tissue which was infiltrated by moderate numbers of plasma cells and lymphocytes. A lymph node from the area was made up of hyalinized connective tissue with central calcification and necrosis and contained organisms with the morphologic characteristics of

*H. capsulatum*. The patient was last seen in October 1957 and was without symptoms.

#### DISCUSSION

McIntire and Sykes (4) showed that chronic mediastinitis was one of the important causes of superior vena caval obstruction, with 16 of the 62 cases in their collected series (1904-46) being classified as idiopathic. The remainder were attributed to syphilis or tuberculosis.

Erganian and Wade (5) felt that these cases of idiopathic chronic mediastinitis constituted an anatomic entity, which they designated as "chronic fibrous mediastinitis." It is with this condition that this paper is concerned. The features displayed in common by the reported cases are a poorly defined mass in the superior mediastinum, composed of dense collagenous tissue, foci of infiltrating leukocytes, and calcification. The etiologic factor was considered to be a mild inflammation of the mediastinum in persons prone to excessive cicatrization. Prior pulmonary infection and trauma were postulated as antecedent factors, but in some of the cited cases the infection or trauma was so remote that their acceptance is difficult, unless re-infection or a smoldering, low-grade inflammatory process is also postulated.

In the light of our present knowledge and techniques, considerable doubt exists regarding the accuracy of diagnosis in those cases which were classified as syphilitic and tuberculous. McIntire and Sykes noted a decline in the number of reported cases of these forms of chronic mediastinitis, but they attributed this to improved methods of control, diagnosis, and treatment. Salyer *et al* found a greater tendency for pathologists to report as idiopathic cases in which laboratory proof was lacking. They also question the validity of diagnosis in earlier cases recorded as tuberculous, on the basis of their experience with over 1,200 pulmonary resections for tuberculosis without evidence of significant mediastinitis, at least of the type with the extensive fibrosis noted in the cases reported above. Auerbach (6) is

quoted as stating that he had never demonstrated tuberculous mediastinitis producing superior vena caval obstruction.

Coincident with the rise in incidence of chronic fibrous mediastinitis, numerous reports appeared in the literature of a newly popular disease—histoplasmosis. This disease was considered for many years to be rare and highly fatal, but suddenly the pendulum of opinion swung to the other extreme. This was largely the result of case finding based on positive skin reactions in asymptomatic individuals. Curry and Wier (7) note this fact and state that the variability of symptoms and the clinical course of histoplasmosis now place it between the extremes of severity and mildness. Silverman and his associates (8), White (9), and many others have also recorded the great variation seen in this disease.

In addition to an apparent skin sensitivity, histoplasmosis has many other characteristics of tuberculosis. A re-infection phenomenon (10, 11) has been noted, and a primary complex is produced which is similar to that of tuberculosis (7, 12-14). These facts emphasize the probability of misdiagnosis. Histoplasmosis may also be mistaken for lymphoma, sarcoid, bronchogenic carcinoma, and many other conditions (7, 15-17).

Criteria for a diagnosis of histoplasmosis are not established. Skin and serologic reactions are questionably specific (8, 9, 18-20), but there has been an overwhelming acceptance in the literature of cases which were diagnosed, in many instances, on little more than a process of exclusion. Silverman *et al* advocate limiting the diagnosis to cases with recovery and culture of *H. capsulatum*. The opinion held here is that each case requires separate evaluation. In some instances, a diagnosis may be warranted without either recovery or culture of the organism. Certainly, identification of the organism in tissue, with corroborative skin and serologic reactions, in the absence of evidence of other disease, should permit acceptance of the diagnosis of histoplasmosis.

It is proposed that this view may be carried still further with respect to chronic fibrous mediastinitis due to histoplasmosis. In the three cases presented above, *H. capsulatum* was described in the biopsy material. The tissue changes correspond to those defined by the entity of chronic fibrous mediastinitis. Four additional patients with chronic fibrous mediastinitis have been recently operated upon at this hospital. In each there was clinical evidence of histoplasmosis, but the organism could not be identified in the surgical specimens. Gillespie (2), in 1956, reported a similar case with superior vena caval obstruction and with excellent clinical evidence of histoplasmosis, but without recovery of the organism. Miller *et al.*, in 1958, reported two cases of superior vena caval obstruction apparently due to fibrosis of the mediastinum incident to histoplasmosis. Neither of these patients came to surgery, but the results of skin tests and serologic reactions, without evidence of other disease, seem to be sufficient for the acceptance of the etiologic diagnosis. *Histoplasmal mediastinitis* is proposed as a designation of these cases of chronic fibrous mediastinitis due to histoplasmosis.

The authors feel that histoplasmal mediastinitis is not uncommon, and that efforts to establish etiologic diagnoses will support their contention, since it seems likely that other reported cases of both the idiopathic and tuberculous varieties were, in reality, due to histoplasmosis. The experience of Salyer *et al.* and of Auerbach support this view. Also, it must be realized that, because of caseating granuloma with calcification, many of the early cases were diagnosed as tuberculosis without demonstration of the organism. This was accepted practice (21-23).

Many authors (7-9, 15, 16, 18, 19, 24-27) have mentioned the unreliability of the diagnosis of histoplasmosis on the basis of roentgen findings. The changes in histoplasmal mediastinitis are no more specific. If, however, the radiologist is alert to

minor changes in the mediastinal shadow, and if he evaluates each case in the light of its clinical history, he is in an excellent position to suggest the course of investigation to be followed to establish the etiologic diagnosis.

Several of the problems of differential diagnosis have been mentioned above. In addition, it would be well to note that, while tuberculosis is the major problem from a numerical standpoint, the preliminary findings in a current study (28) indicate that the immediately pressing problem is a differentiation from bronchogenic carcinoma. Here, skin tests and serologic reactions alone should not be relied upon, for the two conditions have been found to coexist. Jaffe (29) reported a 7 per cent incidence of invasion and obliteration of the superior vena cava in 100 necropsies on patients with carcinoma of the lung. Thoracotomy for diagnosis should not be delayed.

#### SUMMARY

Three cases of chronic fibrous mediastinitis are reported. Each presented different clinical manifestations, and in each case *H. capsulatum* was identified in the surgical specimen. Other similar cases are cited, with apparently valid clinical diagnoses of histoplasmosis, but without identification of the organism.

It is postulated that *H. capsulatum* is an important etiologic agent in the production of chronic fibrous mediastinitis, and that many of the cases previously reported as being tuberculous or idiopathic were, in reality, due to histoplasmosis. The term *histoplasmal mediastinitis* is suggested.

The prognostic value of the extension of the mediastinal mass to the right of the sternum as an indication of future superior vena caval obstruction is suggested.

The nonspecificity of the differential roentgen diagnosis is noted, with special emphasis on the problem of bronchogenic carcinoma.

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## SUMMARIO IN INTERLINGUA

**Chronic Mediastinitis Fibrose Causate per Histoplasma Capsulatum (Mediastinitis Histoplasmal): Reporto de Tres Casos con Differente Symptomas de Presentation**

Es presentate tres casos de chronic mediastinitis fibrose. Omnes exhibiva differente manifestationes clinic, sed in omnes *Histoplasma capsulatum* esseva identificate in le specimen chirurgic.

Es postulate que *H. capsulatum* es un importante agente etiologic in le production de chronic mediastinitis fibrose e que multes del casos previevemente reportate como tuberculosic o idiopathic esseva de

facto causate per histoplasmosis. Es proponite le termino *mediastinitis histoplasmal*.

Es signalate le valor prognostic del extension del massa mediastinal al latere dextere del sterno como indication de futur obstruction del vena cave superior.

Es notate le non-specificitate del roentgeno-diagnose differential, con attention special prestate al problema de carcinoma bronchogene.



## Duodenal Ulcers in Children

With Notes on Their Etiology<sup>1</sup>

JOHN O. LAFFERTY, M.D.

**D**UODENAL ULCERS have been reported in children with increasing frequency (5-11) since Alexander (1) published his group of thirty cases in this journal in 1951, but few of these reports have appeared in the radiologic literature (2). In the same year Morgan (10) also published an excellent review, which thoroughly discussed this condition in children. Many of the more recent papers (3, 6, 12) have stressed the psychiatric factors in the background of these young patients and we have recognized in most of our cases a typical psychologic pattern or have discovered a strong stress situation as a precipitating factor in the production of ulcer.

Since 1949 we have made the diagnosis of duodenal ulcer 15 times in children between two and fifteen years old, out of approximately 92 patients of this age group seen in our office for gastrointestinal studies. This high incidence of positive findings reflects, we feel, not so much a high incidence of disease in this age group as a very conservative attitude on the part of the physicians who refer patients to us for examination. The children must complain for a long time before they are sent for study, and we feel, therefore, that we are dealing with a selected group in which a high percentage of positive examinations may be expected.

The etiology of duodenal ulcer in children, as in adults, is unknown. According to Alexander, "the factors of nervousness, worry, and strain and overindulgence in food, alcohol, or tobacco would seem to play little, if any, part in the production of ulcer in patients of this age." The implication that children have no worries is at variance with our experience, although many of the things that trouble a child would, to an adult, be inconsequential.



Fig. 1. Film showing ulcer crater in a fifteen-year-old girl who had complained of abdominal pain intermittently since the age of six.

A good example of this type of worry and nervous strain is afforded by a four-year-old boy whom we saw in 1951. He had always been well until his parents went to Europe for three months, leaving him and his brother with an aunt. The boy stopped eating, started complaining of severe abdominal pain, and on our examination was found to have a large crater in the duodenal cap. This was treated medically, and after his parents' return his symptoms subsided completely. We saw this child in 1958, after seven years, and he had had no further stomach trouble.

Morgan, after reviewing the various theories of the etiology of ulcer, held the neurogenic theory to be the most tenable. In infants with brain damage, disturbances of the autonomic nervous system controlling centers may cause vascular change in the

<sup>1</sup> From the Radiological Group of Drs. Hall, Lafferty, Coppedge, and Burnett, Charlotte, N. C. Accepted for publication in October 1958.

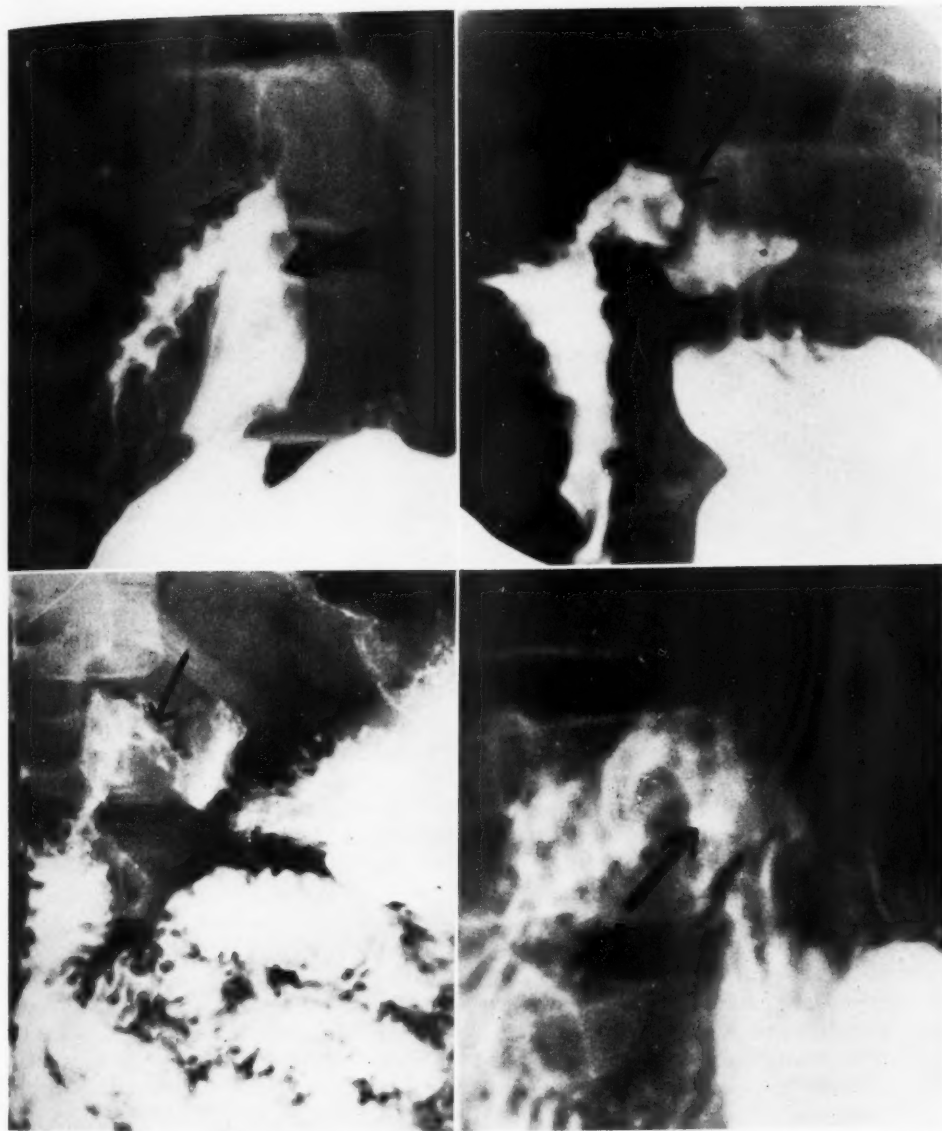


Fig. 2. Selected films from 4 different patients demonstrating the ulcer crater. These children's ages were six to eleven years.

stomach or duodenum sufficiently great to allow erosive lesions to form. In older children with a suppressed anxiety state continued over a period of time, similar vascular changes may be mediated through the autonomic nervous system, leaving the mucosa of the stomach and duodenum open to ulceration.

In many children the gastrointestinal tract responds regularly to stress situations with an ulcer or ulcer-like reaction. A seven-year-old girl whom we first saw in 1949, shortly after she started to school, complained of abdominal pain and vomiting of sufficient severity to cause her pediatrician to ask for a gastrointestinal series.

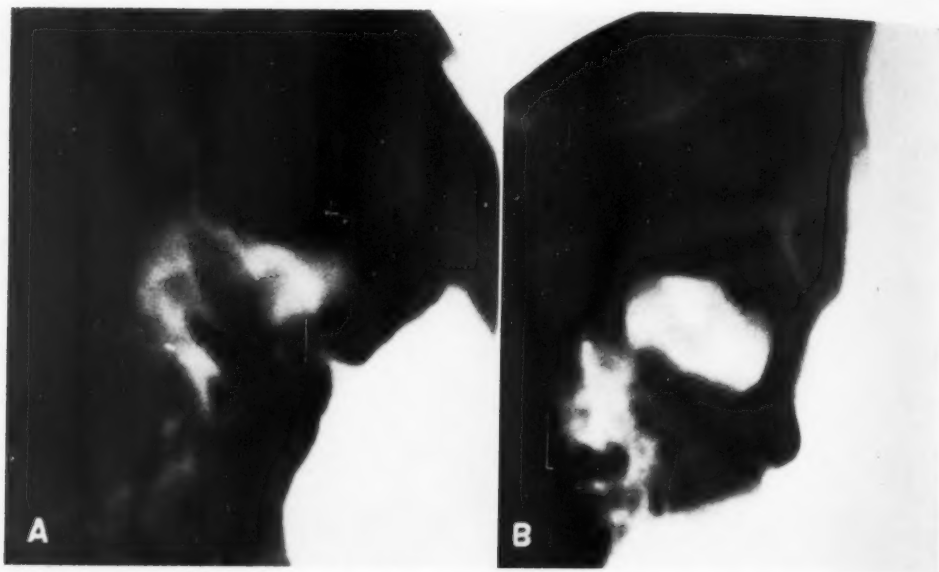


Fig. 3. Case I. A. Ulcer crater found in a four-year-old girl. B. Recurrence three years later, following birth of sibling.

This was negative. Under symptomatic treatment the symptoms subsided and the patient had no further trouble until 1957, when we saw her a few months after she entered high school, at the age of fifteen. Again her complaint was abdominal pain and vomiting every morning before school, whenever she was going out on a date, and at other times of stress. Examination at this time showed a superficial ulcer in the duodenal cap (Fig. 1). Ulcer therapy controlled her symptoms, and at the time of this report she was becoming well adjusted to her new school situation.

The symptoms of which these children complain are not at all those of the "typical" adult ulcer patient. Hunger pain and food relief are rare. Most often there is generalized abdominal pain, sometimes with vomiting, the latter recurring regularly at a particular time of day, which differs with the individual. Occasionally there will be bleeding. As the child grows older, the symptoms become more typically adult. Some gastroenterologists feel that a certain number of their adult ulcer patients had ulcers as children, and it is true that older persons with well developed

ulcers and scarred caps are often found, on questioning, to have had many stomach-aches in their childhood years, or to have been characterized as "a child with a weak stomach."

The diagnosis, of course, must be made radiographically, and the technic is similar to that used in adults. The children are given unflavored barium if possible, but occasionally chocolate syrup is added to prevent emotional reactions (4). Meticulous fluoroscopy is necessary and we take many spot films. A crater must be seen, as the diagnosis is not tenable when the findings are limited to spasticity and irritability. There will be no scarring of the cap and no clover-leaf deformity as in adults, but often a halo is seen around the crater (Fig. 2). These findings are reproducible in subsequent examinations. Mucosal-relief roentgenograms are often of inestimable value.

The treatment of children with ulcers is similar to that of adults; a bland diet with frequent feedings, mild sedation, antacids, and reassurance. Psychiatric help for the child and his parents is often of value in resolving an underlying conflict.

The results are almost uniformly good, and none of our patients has required surgical intervention.

Chapman, Loeb, and Young (3), in their complete psychosomatic study of 5 children with ulcer, found a definite personality pattern in this small series. They group their findings in three categories: (1) unmet need for affection and emotional security, (2) difficulties in being assertive of their hostile feelings, (3) resultant passivity and subnormal assertiveness, with a desperate need to secure affectionate approval from the persons around them. Taboroff and Brown (12) made similar observations in a group of 6 patients, whom they studied completely.

Girdany (6), in reporting 45 ulcers, stated that the children were tense and bright but lacked overt emotional lability. The parents often said of these children that they didn't express their feelings and described them as introverts. Girdany also pointed out the fact that there was frequently a precipitating factor in producing the symptoms.

Two of our patients who have had complete psychosomatic studies fit into the emotional pattern described by Chapman, Loeb and Young, and by Taboroff and Brown:

**CASE I:** A four-year-old girl was first found to have a duodenal ulcer in 1951 (Fig. 3, A), following an automobile accident in which the family was involved and about which the patient was greatly concerned for some time. This ulcer did not respond well to treatment, and there was an acute exacerbation following the birth of a sibling (Fig. 3, B). The ulcer bled on several occasions necessitating blood transfusions.

Psychiatric help for the family and the child was requested. The psychiatrist found that her behavior was constricted by a compulsive need to be proper, adequate, and acceptable. The mother insisted on extreme neatness, and the parents were proud of their sweet, submissive child, and of the neatness which she developed in her play activities. They seemed to feel that placid, quarrel-free home was preferable to a spontaneous one. The patient, according to the examiner, obviously felt the opposite but stringently adhered to the demands of others. The ulcer improved when she was able to break through her studied constrictiveness and express natural impulses without retaliation, direction, or correction.



Fig. 4. Case II. Ulcer crater in nine-year-old boy.

The younger sibling, now three, is under treatment at the Charlotte Mental Health Clinic, with autistic disorder, and the examiner felt that the enforced submissiveness to the demands of the schizophrenogenic mother for placidity were leading to autism in one child and psychovisceralization in the other. It is interesting that ulcer symptoms in the older child improved more rapidly as the mother became preoccupied with the demands of the second child, who was aggressive and demanding.

This patient also probably had a gastrointestinal allergy to milk. This was tested with a barium meal, followed by milk. A marked change occurred in the small bowel within ten minutes, with some pain, necessitating Demerol for relief. This may have delayed the healing of the ulcer. One cannot rule out completely the possibility that this response was emotional in origin.

**CASE II:** A nine-year-old boy with a mild spastic paraplegia was seen in 1955 complaining of generalized abdominal pain without any physical findings. Our examination showed a shallow ulcer crater (Fig. 4). The child was placed on a bland diet and antacid therapy with marked improvement. One year later he was seen by the Mental Health Clinic because of difficulty at school. He was described as a child consumed by a need for unsolicited approval and relief from the conflict which

had developed over the need for constructing his life to deserve approval and love. He was quite hostile to his parents, especially to his father, who represented the fact that his son's physical handicap prevented excelling in sports. Psychiatric treatment was recommended but was not undertaken. The child, however, was examined in the past month and found to have no ulcer.

#### SUMMARY

Duodenal ulcers occur in children much more frequently than has been appreciated in the past. The symptoms differ from those in the adult patient, but radiographically a crater can be found.

Many of these children have deep-seated psychiatric problems and help in these will do much to bring about improvement.

Results of non-surgical treatment are good but it is felt that a certain percentage of adult ulcers have their roots in childhood.

Illustrative cases are reported.

ACKNOWLEDGMENT: I express my thanks to the following for referring patients to us and giving us the clinical information concerning them: Drs. E. K. McLean, F. R. Cochrane, M. L. Rutledge, A. R. Gunter, W. E. White, and M. T. Gilmour, and to Dr. Marshal Fisher at the Charlotte Mental Health

Clinic, who furnished the information about the psychiatric findings in the two cases.

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#### SUMMARIO IN INTERLINGUA

#### Ulcères Duodenal in Juveniles, con Notas Super Lor Etiologia

Ulcères duodenal occurre in juveniles multo plus frequentemente que esseva supponite in le passato. Le symptomata differe ab illos in patientes adulte, sed radiographicamente un crater pote esser trovate.

Multes de iste juveniles ha profunde

problemas psychiatric, e adjuta con respecto a istos contribue grandemente al melioration del ulcères. Le resultados de tractamento non-chirurgic es bon, sed il pare que un certe procentage de ulcères in adultos ha lor origine durante le pueritia.

Casos illustrative es reportate.



# Functional Disturbances of the Gastrointestinal Tract<sup>1</sup>

THOMAS E. MACHELLA, M.D.

PATIENTS WITH symptoms attributable to functional motor disturbances of the gastrointestinal tract are frequently encountered. Often they are subjected to a variety of laboratory and x-ray procedures but, because no evidence of organic disease is found, are offered no satisfactory explanation for their symptoms other than that these are due to "nerves." In the majority of such instances, the correct diagnosis may be made by an evaluation of the presenting symptoms in terms of physiological changes and an elucidation of the underlying emotional disorder suggested by their presence. The radiologist may be of invaluable assistance in the diagnosis by calling attention to and reporting all motor disturbances encountered during his examinations.

The basic set-up for the development of functional motor disturbances consists of the brain, the autonomic nervous system, and the effector organs. The brain is capable of receiving various auditory and visual perceptions which, on the basis of interpretation, can give rise to certain emotional states. These emotional states, in turn, cause autonomic reactions in the brain, which transmits impulses to the viscera by way of the two divisions of the autonomic nervous system, the sympathetic and the parasympathetic. The autonomic nervous system innervates the effector end plates of the various viscera where inhibition or excitation of function occurs.

It is generally accepted that the functions of the two divisions of the autonomic nervous system are mutually antagonistic, the parasympathetic being excitatory to the gastrointestinal tract (except its sphincters), while the sympathetic has the reverse influence. Among the stimuli

which are apt to excite the parasympathetic nervous system are hostility, anger, hate, and resentment, while the sympathetic is influenced by anxiety, fear, worry, and sadness.

Drugs which excite the parasympathetic nervous system are referred to as cholinergic, and of these the most clinically useful is Urecholine. Drugs which depress the parasympathetic nervous system are referred to as anti-cholinergics and comprise atropine, Elorine, Pro-banthine, Darbid, and many others, including belladonna preparations.

In this presentation, an attempt will be made to relate clinical manifestations to disturbances in motor function of the gastrointestinal tract in patients in whom a relationship has been established between the development of symptoms and stressful life situations involving basic conflicts, character defenses, and maladjustments in social, occupational, economic, marital, and sexual fields. It must be pointed out that the mechanisms of the symptoms are adduced partly from inference based on clinical observation and partly from experimental evidence.

## THE ESOPHAGUS

The motor disturbances of the esophagus which appear to be precipitated by stressful emotional disturbances are esophagospasm and achalasia, both of which may be responsible for dysphagia. Neither of them is to be confused with globus hystericus, a paresthesia referable to the pharynx and interpreted by the patient as "a lump in the throat," which occurs in response to an emotional stimulus such as grief or sadness.

*Esophagospasm:* Spasm of a segment of the lower esophagus may occur during

<sup>1</sup> From the Gastro-Intestinal Section (Kinsey-Thomas Foundation) of the Medical Clinic of the Hospital of the University of Pennsylvania, Philadelphia 4, Penna.

Presented at the Forty-third Annual Meeting of the Radiological Society of North America, Chicago, Ill., Nov. 17-22, 1957. Received for publication in April 1959.

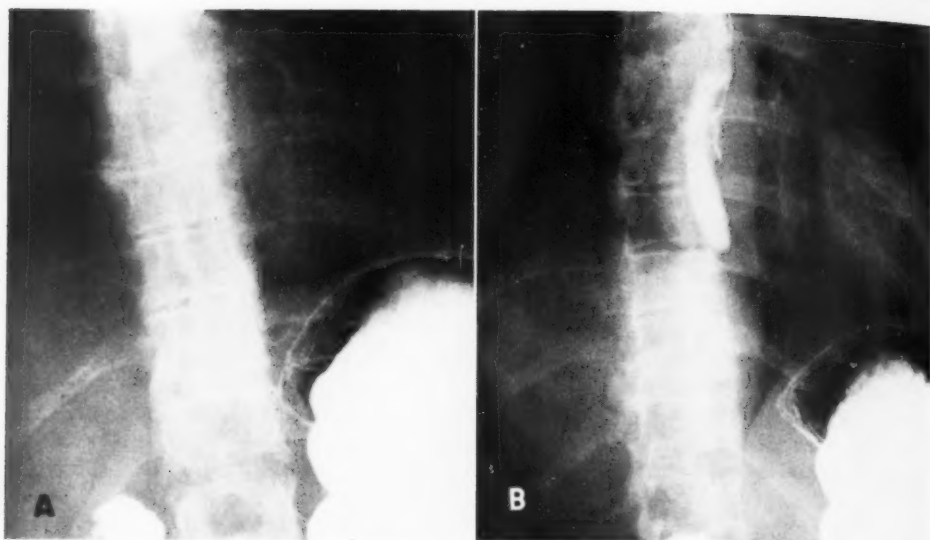


Fig. 1. Esophagospasm. The spastic segment of esophagus above the cardia is longer in film A than in B, which was exposed later. The esophagus is not dilated above the area of spasm.

emotional stress, especially while eating. This condition is called esophagospasm and results from an excessive parasympathetic influence. It is not associated with dilatation of the esophagus and is not to be confused with achalasia. Radiologic examination may reveal nothing abnormal, unless the patient is upset or made to feel insecure during the procedure, when spasm may be noted (Fig. 1).

The symptoms of esophagospasm include not only dysphagia, but also discomfort beneath the sternum. When observed during an episode at meal time, the patient may be suspected of having a heart attack; he stops eating, breaks out into a sweat, and appears apprehensive until the sensation disappears. The substernal pain may be quite severe. Such persons usually develop a fear of eating in company or in public places because of possible embarrassment.

Occasionally, the attack occurs during a troubled sleep. The patient awakens with severe substernal pain which lasts a few minutes to an hour. Again, a heart attack may be suspected. The clue to the esophageal origin of the pain lies in the associated dysphagia.

Results of drug therapy are quite satisfactory in the treatment of esophagospasm. Anticholinergic and sedative drugs administered before meals which are to be eaten under stress will usually prevent the spasm. They should be taken before all meals if those which will be eaten under stress cannot be predicted. Once the spasm has occurred and pain is severe, an injection of Demerol or an effective anticholinergic drug will usually terminate the attack promptly.

*Achalasia:* Achalasia, often called cardio-spasm, is a disorder of the esophagus in which swallowed material does not enter the stomach. Radiologically, a spindle-shaped narrowing within the distal 5 cm. or less of the esophagus is seen (Fig. 2). The lower end is obstructed. Above the narrowed segment, there is dilatation of various degrees depending on the duration and frequency of the episodes. A failure of the cardia to relax, rather than an actual spasm of the sphincter, is believed to be responsible for the inability of ingested material to enter the stomach. An abnormality of the motor activity of almost the entire esophagus may be demonstrated by fluoroscopic and balloon

kymographic methods. Pressure recordings in the dilated esophagus show decreased muscular tone, irregular phasic activity, and absence of the propulsive peristaltic wave (58). When such a patient is given Mecholyl, violent tonic contractions appear that are not seen in normal subjects or in patients with other esophageal lesions. The response includes obliteration of the lumen and substernal pain (58). A gastric tube or esophagoscope can often be passed into the stomach without meeting resistance at the cardia, particularly when the patient is not under the stress responsible for his episodes of dysphagia. It is also of interest that discomfort due to the retention of food in the esophagus may be lessened by drinking a glass or two of fluid, thereby causing the esophageal content to pass into the stomach by force of gravity.

As far as the role of the autonomic nervous system in achalasia is concerned, experimental evidence suggests that the motor disturbance is due to a removal of parasympathetic influence on the esophagus, including the cardia. The condition has been produced in cats by bilateral vagotomy (59). It has also been reported to occur following injury to the ganglion cells of Auerbach's plexus by injection of phenic acid between the muscle coats (22), as well as in injury of the plexus by inflammation as a result of infestation with *Trypanosoma cruzi* (56).

Numerous writers report absence of the ganglion cells "from the esophagus" and many state that the condition is similar to that which exists in the aganglionic segment in the rectum or rectosigmoid in Hirschsprung's disease or congenital aganglionic megacolon. The comparison is confusing, since the narrowed segment in achalasia is said not to be in spasm, but rather to represent a failure of the sphincteric region to relax; on the other hand, that the narrowed segment in congenital aganglionic megacolon is in spasm is generally accepted. The situation is further complicated by the recent report of Trounce *et al.* (88), who found ganglion

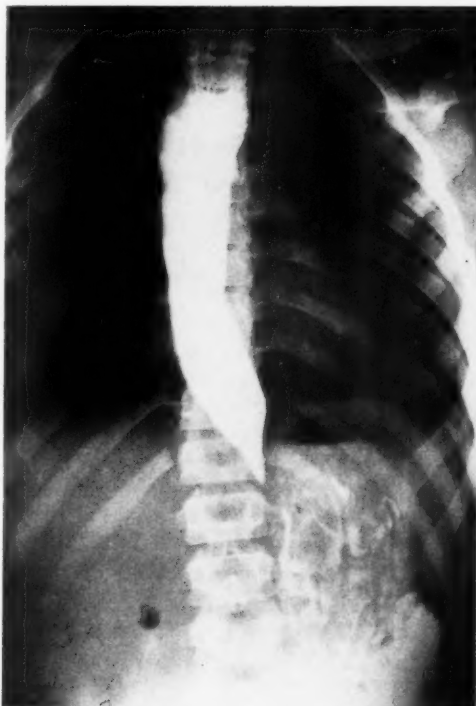


Fig. 2. Achalasia of the esophagus. The "narrowing" is at the cardia and the esophagus above is dilated in contrast to the appearance in esophagospasm.

cells in the lower segment of the esophagus, including the cardia, in 4 to 6 patients with achalasia.

Additional evidence suggesting that the parasympathetic division of the autonomic nervous system is at fault lies in the observation that in some cases of achalasia there appears to be a simultaneous derangement of pyloric function, resulting in gastric stasis which may predispose to a reflux esophagitis following surgical procedures on the cardia. Also, achalasia and Sjögren's syndrome are occasionally associated (93). A derangement of the parasympathetic influences on the salivary glands has been thought to be responsible for some instances of Sjögren's syndrome.

The importance of the role of emotional factors in achalasia has been emphasized by many. They were mentioned as early as 1733, when Hoffman (48) ascribed the disorder to "irrational love" and "un-

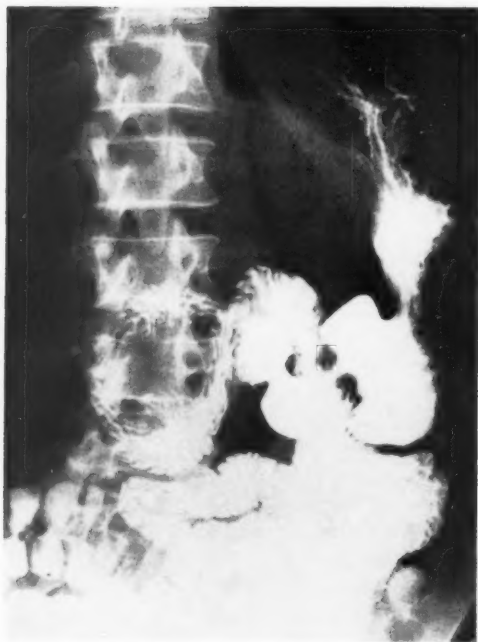


Fig. 3. Gastric hypermotility and rapid gastric emptying associated with a rapid rate of small intestinal transport. Barium has reached the colon in about fifteen minutes after the ingestion of the barium meal.

controlled desires." Since that time considerable clinical evidence has been accumulated to indicate that the disorder occurs in response to stressful life situations. Studies of the psychosomatic aspects of achalasia demonstrated that neurotic traits were frequently observed during childhood and in many instances persisted into adult life (70). Patients with achalasia have been characterized as perfectionists, neat, orderly, and meticulous. They have also been described as submissive, sensitive, and rather easily offended. McMahon *et al.* (70) reported that cardiospasm is a disease of frustration and is not seen in happy, contented, or well adjusted persons. A motility pattern including dysrhythmia, with delay in passage of ingested barium into the stomach, has been produced in susceptible normals by the discussion of troublesome personal conflicts (102).

Clinically, the onset of dysphagia occurs during a change in the emotional status

of the patient and at first the symptom occurs only during meals eaten under stress. Esophageal pain of varying intensity and character has been reported in from 30 to 60 per cent of the cases. It occurs more frequently when the esophagus is only slightly or moderately dilated. Substernal or epigastric discomfort in the form of a feeling of weight or oppression due to retained food is common. Belching and vomiting of undigested food occur frequently. After numerous and repeated episodes, dysphagia becomes nearly constant, and the esophagus is not only dilated but elongated and eventually reduplicated and "S"-shaped to cause the familiar appearance of megaesophagus. Progressive loss of weight with severe malnutrition and dehydration ensues.

The results of drug therapy in achalasia are unsatisfactory. Anticholinergic drugs and Benzedrine are ineffective. Inhalation of amyl nitrite or absorption of nitroglycerine from the sublingual mucous membranes early in the disease may cause almost immediate disappearance of the stenosis at the lower end of the esophagus, with passage of esophageal contents into the stomach (79). These drugs, however, are not ideal for continued use because of unpleasant side-reactions. Best results are obtained early in the course of the disease, with the discovery and solution of the underlying emotional problems. When this has not been accomplished and the process has continued, bougienage or surgical procedures on the cardia may be necessary. The fact that dysphagia is relieved by bougienage or an operation such as the Heller procedure (myotomy of the lower end of the esophagus and adjacent portion of stomach), gives strong support to the view that an abnormality of the cardia is an important factor in the dysphagia.

#### THE STOMACH

A relationship between the emotional state and the behavior and appearance of the gastric mucosa was observed by William Beaumont in Alexis St. Martin.

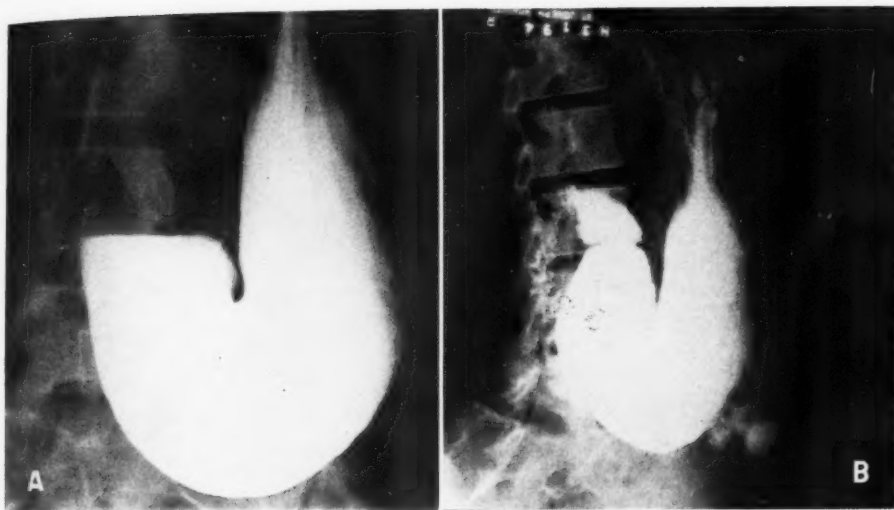


Fig. 4. A. Initial delay in gastric emptying ascribed to apprehension on the part of the patient. The stomach is somewhat atonic and devoid of peristalsis.  
B. The stomach began to empty about six minutes after film A was exposed.

Beaumont (11) noted that undue excitement, fear, anger, or "whatever depresses or disturbs the nervous system" was associated with a disturbance in the appearance of the villous coat. Wolf and Wolff (101) also observed that emotional disturbances altered the behavior and appearance of the mucosa in their gastric fistula subject, Tom.

**Gastric Hyperactivity:** Hostility, unexpressed anger, rage, resentment, and generally an aggressive behavior have been observed to cause hyperemia of the gastric mucosa and an increase in secretory and motor activity (101). This is a parasympathetic type of response and has been noted in animals as a result of electrical stimulation of the peripheral end of the vagus. Such an effect was also reported by Cushing following direct stimulation of the tuber nuclei in the hypothalamus or its descending tracts. Cushing (21) ascribed the gastric response to a functional release of the vagus from the paralysis of antagonistic sympathetic fibers. Similar abnormal gastric physiological changes consisting of hypersecretion, hypermotility, hypertonus, and rapid gastric emptying may be observed in association with active

duodenal ulcer. They can be reversed by a complete bilateral vagotomy performed at the level of the diaphragm and may be restored temporarily by an injection of Urecholine.

Gastric hypermotility (Fig. 3) in the absence of obstruction to the outlet of the stomach is usually not responsible for symptoms. Occasionally, however, manifestations of the "dumping" reaction occur when a meal rich in foods with high osmotic properties is eaten under stress and promptly emptied into the small intestine without having been subjected to the usual mixing, dilution and partial digestion in the stomach. In such cases the "dumping" reaction may be prevented and gastric emptying prolonged by the oral administration of an effective dose of an anticholinergic drug before meals.

**Gastric Hypoactivity:** Fear, sadness, depression, dejection, disgust, and a feeling of being overwhelmed are generally looked upon as causing a sympathetic type of response, *i.e.*, gastric hypofunction, ischemia of the mucosa, decreased secretory activity, diminution or absence of peristalsis, and delayed gastric emptying. An initial delay in gastric emptying is not





Fig. 5. Prolonged gastric retention in the absence of obstruction at the outlet of the stomach in a patient saddened by the death of her mother. The stomach is somewhat atonic and devoid of peristalsis. There is no organic obstruction at the outlet of the stomach.

infrequently encountered at the beginning of a fluoroscopic examination in the patient who is afraid of what may be found (Fig. 4).

Clinically, evidence of sympathetic hyperactivity has been encountered in individuals saddened by grief, as by the death of a loved one. In such instances gastric retention has been noted in association with anorexia, belching, nausea, and vomiting (Fig. 5). The gastric retention may be prevented by the administration of the parasympathomimetic drug, Urecho-line (68), in doses of 5 to 10 mg. subcutaneously or sublingually, and less effectively by doses of 35 to 50 mg. orally, before meals.

#### THE DUODENUM

Functional motor disturbances of the duodenum include spasm and stasis in the second and third portions.

*Spasm of Descending Limb of Duodenum:* Spasm of the postbulbar or descending limb of the duodenum (Fig. 6) is sometimes encountered in the absence of a demonstrable postbulbar ulcer. The spasm, a parasympathetic type of response, may be associated with nausea, vomiting, and pain and tenderness in the epigastrium. It may be relieved by the injection of an

effective dose of an anticholinergic drug and, when it occurs frequently, may be prevented by the regular oral administration of such a compound before meals. Bercovitz (13) has recently published results of an analysis of 230 cases and has referred to the condition as the postbulbar duodenal spasm syndrome.

*Megaduodenum (Duodenal Stasis):* A disturbance in tonus and of motility with stasis proximal to the involved point may be encountered in the duodenum. Fonseca (32) has differentiated three forms of megaduodenum: megalobulbus without enlargement of the other duodenal segments, enlargement of the duodenal arch, and total megaduodenum, with a gigantic duodenal arch. Of these the second is the most frequently encountered, *i.e.*, stasis in the segment proximal to the junction of the third and fourth portions. In milder instances (Fig. 7) the disturbance, as observed fluoroscopically, consists of stasis and occasionally a "to-and-fro" movement of the barium. More severe degrees of the disorder are associated with marked retention of barium in the dilated proximal loop of the duodenum (Fig. 8). Such severe degrees of stasis often have been attributed to compression of the junction of the third and fourth portions of the duodenum by the superior mesenteric vessels, the so-called superior mesenteric artery syndrome.

Certain observations, however, have raised doubt as to whether such stasis is always due to obstruction by mechanical compression by the superior mesenteric artery or whether the disturbance, as suggested by Abbott (1), is due to a functional change in the duodenal musculature. These observations include failure to relieve the stasis by lying on the abdomen, thereby relaxing tension of the vessels on the duodenum, the fact that certain persons have irregularly occurring episodes of stasis associated with anorexia, nausea, and vomiting when they are emotionally disturbed (97), the total disappearance of the phenomenon in some patients (1), and the better results from

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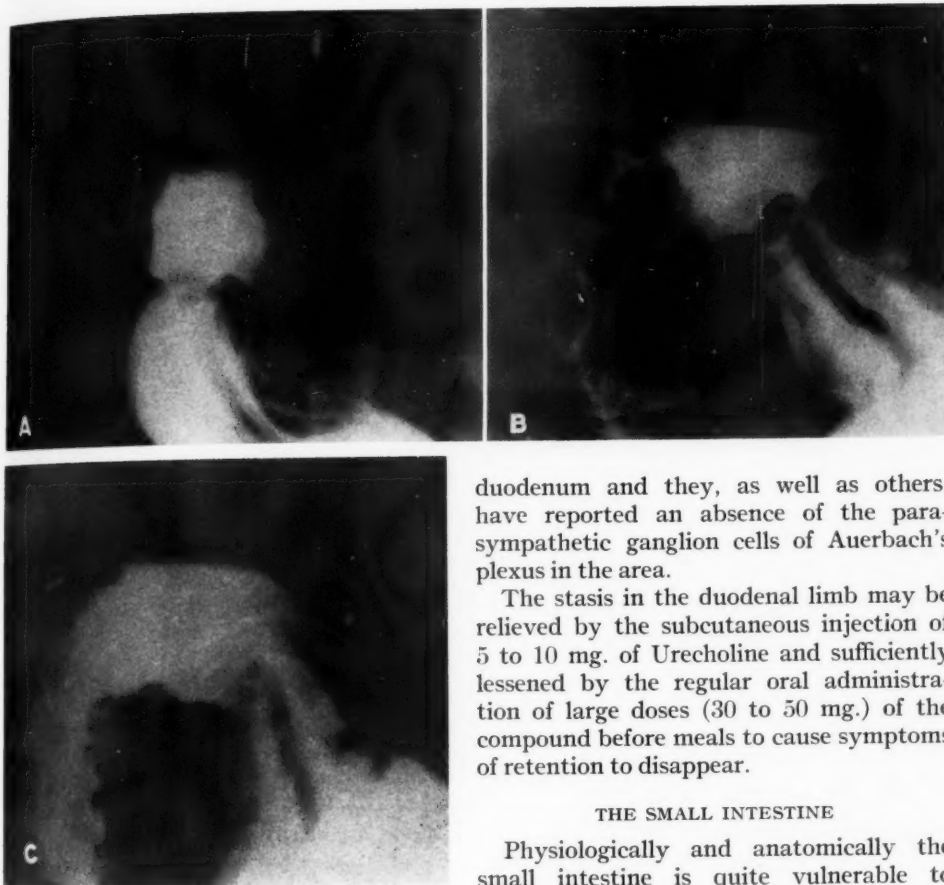


Fig. 6. A. Spasm of the descending limb of the duodenum. No barium is seen in the loop.  
B. A thin stream of barium is seen shortly afterward, as the loop began to relax.  
C. Wide stream of barium in the now more relaxed loop.

medical management than from surgical short-circuiting procedures (17). Some writers have felt that the mechanism of the disorder based on a neuromuscular defect is rather similar in nature to that in megacolon, megaesophagus, and megaureter, and indeed patients have been encountered in whom more than one of these conditions coexisted. Fonseca (32), for example, found megaduodenum in 30 per cent of his patients with megaesophagus. Barnett and his associates (9) feel that the stasis results from a neuromuscular disturbance in the wall of the

duodenum and they, as well as others, have reported an absence of the parasympathetic ganglion cells of Auerbach's plexus in the area.

The stasis in the duodenal limb may be relieved by the subcutaneous injection of 5 to 10 mg. of Urecholine and sufficiently lessened by the regular oral administration of large doses (30 to 50 mg.) of the compound before meals to cause symptoms of retention to disappear.

#### THE SMALL INTESTINE

Physiologically and anatomically the small intestine is quite vulnerable to

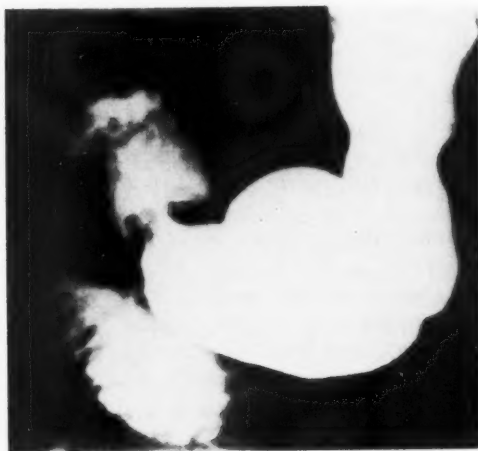


Fig. 7. Example of mild stasis in proximal duodenal loop.

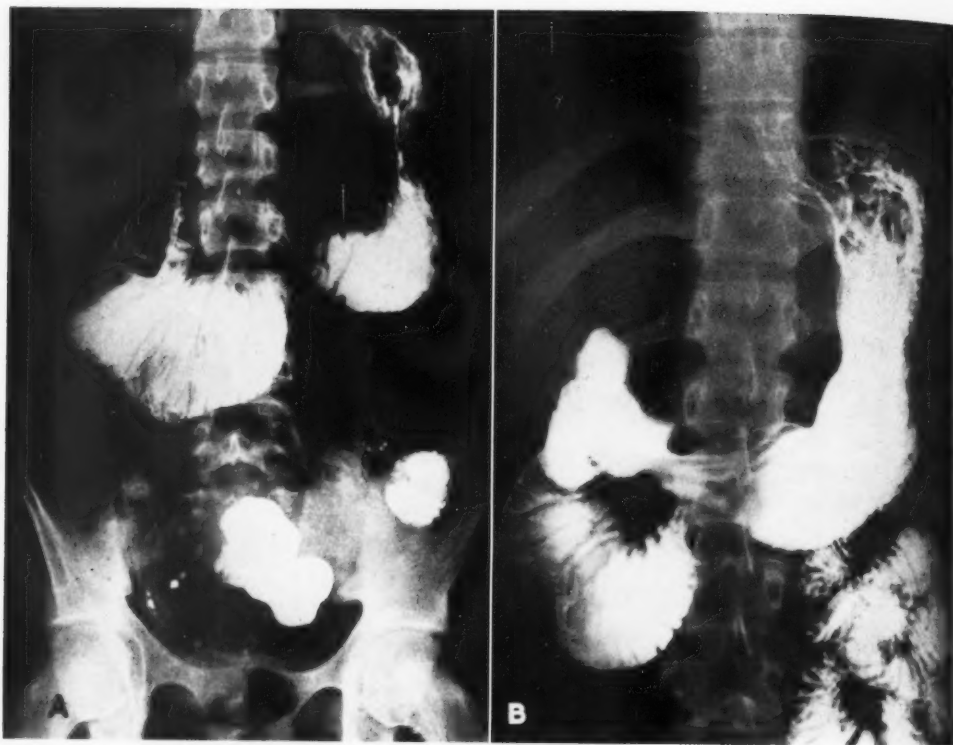


Fig. 8. A. Example of marked stasis in the proximal duodenal loop.  
B. Less marked stasis in the duodenal loop at a time when symptoms of retention were much less manifest than when film A was exposed.

instability and derangement. Its susceptibility to emotional disturbances has been noted by numerous investigators (26, 40, 51, 66, 68, 81, 83). Alterations in the mucosal pattern induced by emotional stress have been reported by Friedman (33). Increased motor activity has been demonstrated by the balloon kymographic method, and hyperemia and increased mucosal fragility have been noted in persons subjected to stress interviews (20). A stimulating effect of emotional tension on small bowel activity was observed by Weeks (91), who studied the exposed ileum of a wounded Arab.

**Hyperactivity:** Hypermotility of the small gut as a result of stressful life situations is often an important factor in the diarrhea associated with irritable colon. It is frequently associated with gastric hypermotility and rapid gastric emptying (Fig. 9). The ingestion of food also

causes an increased motor activity of the distal small intestine, the gastroileal reflex (23). In such instances, the patients are subjectively conscious of increased intestinal activity and may even experience an urge to defecate during or shortly after meals. The stools may be dark green in color, because the bile pigments have not had sufficient time to be altered by the bacterial flora of the colon, and may also contain food which ordinarily would have been digested. Such rapid transit through the small intestine in certain cases of diarrhea was reported by Golden in 1936 (40), and more recently by Kalser *et al.* (52).

Pain of small intestinal origin occurs from spasm or distention of the musculature. It has been observed in the absence of a colon and is interpreted by the patient as cramps or "gas pains." Areas in which pain resulting from distention of a balloon

in the small intestine have been charted by Miller, Abbott, and Karr (72). These are characteristically referred to the periumbilical region, pain from the jejunum being referred to a point above the umbilical line and from the ileum to a point below that line. The efferent pain fibers travel in the sympathetic system and sympathectomy abolishes pain on the ipsilateral side.

Anticholinergic drugs are quite effective in decreasing motor activity and slowing the rate of transport in the small intestine. Their administration before meals will usually abolish the diarrhea and cramps when these are due to small intestinal hypermotility, though such drugs also tend to depress gastric and colonic motor hyperactivities.

*Hypoactivity:* Theoretically, decreased motor activity of the small intestine should occur in response to the emotional stimuli of the sympathetic type, such as fear and sadness. Actually it occurs during natural sleep (46), after barbiturates and anticholinergics, in association with invasive retroperitoneal neoplasm including carcinoma of the pancreas, in sprue, and in diabetics when the blood sugar is elevated. It has been noted also in certain cases following vagotomy.

Hypomotility of the small intestine in the absence of sprue or adynamic ileus usually does not cause distinctive symptoms with the exception of flatulence. In the presence of associated gastric and colonic hypomotility, it is difficult to decide just which portion of the gastrointestinal tract is responsible for the symptoms. Cholinergic drugs, such as Urecholine, are effective in increasing motor activity as well as the rate of transport in the small intestine.

Evidence of stasis in the distal ileum is not infrequently encountered in persons in whom the mouth-to-cecum time is being estimated radiologically for experimental purposes. This has been a troublesome factor in gauging small intestinal transport time exactly. Not infrequently the head of the barium column reaches to

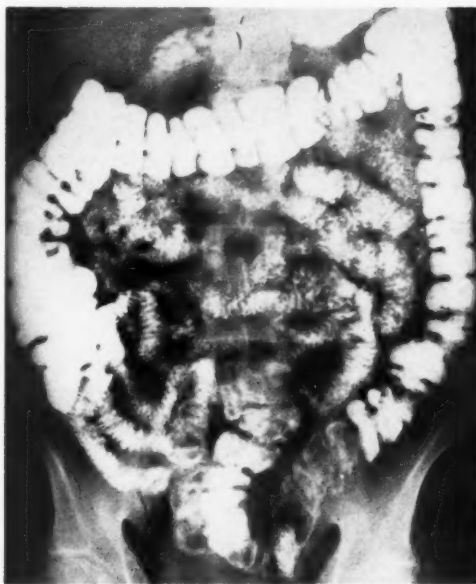


Fig. 9. Rapid rate of transport in the small intestine and colon. Film was exposed about fifteen minutes after ingestion of a standard barium-water meal.

within a few inches of the ileum in a matter of minutes but fails to progress further for hours. The inference is that spasm of the terminal ileum is responsible, though some feel that actual stasis exists and refer to the abnormality as the "iliac stomach."

#### COLON

The colon is divided into two parts according to its physiological function, embryological derivation, and blood supply. The right half is derived from the embryonal midgut, has primarily an absorptive function, contains material which is comparatively fluid in consistency, and receives its arterial blood from the superior mesenteric artery. The source of its parasympathetic innervation is not clear. The left half is derived from the embryonal hindgut, has primarily a storage function, contains material which is relatively solid in consistency, receives its arterial blood from the inferior mesenteric artery and its parasympathetic innervation from the 2nd, 3rd, and 4th sacral nerves. The pelvic portion of the left colon serves as



a storehouse for feces which, when transferred into the rectum, initiate the defecation reflex by distention.

Ordinarily the colon empties a standard opaque meal in about forty-eight to seventy-two hours (53). The motor activities of the colon, including mass peristalsis, can be initiated by the taste, smell, thought, or ingestion of food, by certain types of emotional stress, and by cholinergic preparations. It is depressed by sleep (80) and certain drugs, including opiates and ganglionic blocking agents.

The gastrocolic reflex consists in an increase in colonic motor activity following the ingestion of food. The passage of food through the pylorus and into the upper small intestine causes entry of ileal contents into the cecum, this also increasing activity in the large intestine. The gastrocolic reflex may be exaggerated in some instances and be responsible for abdominal cramps and one or more bowel movements after meals.

In general it has been found that during anger, resentment, or hostility the mucosa becomes hyperemic, engorged, and hyperactive, while during periods of comparative calm and tranquillity it is pale and relatively inactive (42, 43, 96). Pain, fear, and anxiety have been found to produce pallor of the mucosa and to inhibit motility (96).

The changes in appearance of the sigmoid colonic mucosa in response to anger, resentment, and hostility are similar to those of the stomach, *i.e.*, hyperemia and hyperactivity. Such appearances can be induced by stimulation of the parasympathetic nerve supply of the colon in animals (39), as well as by the injection of parasympathomimetic drugs, such as Mecholyl (95), acetylcholine, and Prostigmine (64), suggesting that the parasympathetic nervous system is primarily excitatory to the colon. Certain observations, however, indicate that the sympathetic nervous system also may contain excitatory fibers. Schlitt *et al.* (82), for example, found that neither sacral parasympathectomy nor vagotomy produced

any detectable change in basic motility of the distal colon and that it could be eliminated only after a combined sympathectomy and sacral parasympathectomy. The work of these investigators, as well as that of Wells *et al.* (94), casts doubt on the commonly accepted view of the antagonism of the two components of the autonomic nervous system in respect to the distal colon. As a matter of fact, in some instances, stimulation of the sympathetics has produced predominantly motor responses (94). Consequently, in view of these variations and the differences in innervation of the two halves of the colon, it might be expected that the end reaction in the colon in response to stress stimuli may vary from person to person, and even in the same person, depending on several factors, such as the following:

1. The relative strength and effectiveness of the two effector divisions of the autonomic nervous system in a given person. There is a tendency for one or the other division to be dominant, and often personality and behavior patterns are established at an early age which become characteristic throughout life.

2. The nature of the emotional stimulus. The emotions to which men are subjected throughout their lives are many, including anxiety, fear, worry, need for approval and recognition, hostility, anger, hate, aggression, inferiority feelings, guilt, ambivalence, ambition, and envy.

3. The intensity, duration, and frequency of the emotional stimulus.

4. The combined action of several stimuli with opposite effects operating simultaneously or closely together.

5. The ability to accept and adjust to a disturbing situation on the basis of a philosophy gained from experience and maturity.

6. The capacity to ventilate problems and "get things off one's chest."

7. The ability to settle problems promptly, thereby avoiding prolonged brooding.

8. The threshold for stress, *i.e.*, the



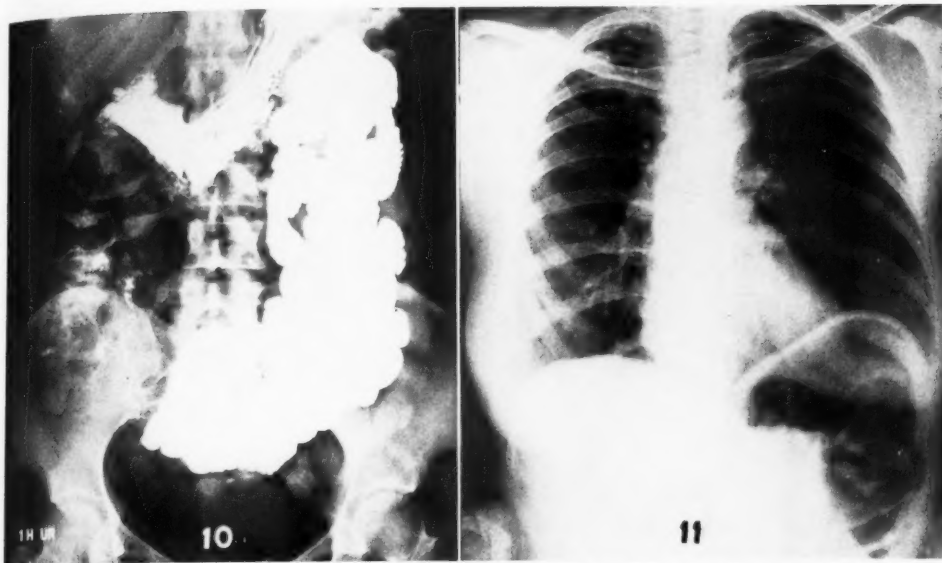


Fig. 10. Distention of right side of colon responsible for attacks of right-sided abdominal pain. Large bubbles of gas mixed with feces can be seen in the distended proximal colon.

Fig. 11. Roentgen appearance of splenic flexure distended with gas. The patient experienced attacks of pain in the left upper quadrant of the abdomen referred to the precordium and left shoulder, relieved by expulsion of flatus or feces.

sensitivity of the reactor to adverse life situations.

### Clinical Disturbances

The colon, being susceptible to many types of extrinsic and intrinsic stimuli by virtue of its muscular excitability and pain responses of varying thresholds, receives the brunt of emotional stimuli in many individuals. Consequently, it is not surprising that different clinical pictures occur. Classified according to changes in bowel habits, they consist of constipation, diarrhea, and alternating constipation and diarrhea, each of which may or may not be associated with pain.

1. *Hyperactivity of Colon:* (a) *Constipation with Pain:* Abdominal pain associated with constipation may be of several types and may occur in practically any area of the abdomen occupied by the colon.

There may be *pain in the left lower quadrant* due to prolonged spasm of the descending colon. Tenderness on palpation over the spastic segment is invariably present.

Attacks of *pain in the right side of the abdomen* may occur as a result of distention of the cecum and the ascending colon (Fig. 10). In such patients, spasm is usually present in the proximal transverse colon. Sometimes, the entire proximal and transverse colon distends as a result of spasm of the descending colon. In these cases, currently available anticholinergic drugs are relatively ineffective. The spasm can be relieved by an injection of Demerol, but the repeated use of this drug may lead to addiction.

Attacks of *pain in the left upper quadrant* due to distention of the splenic flexure by gas or feces constitute the so-called "splenic flexure syndrome" (Fig. 11). The pain from distention of the splenic flexure may be referred to several sites above the diaphragm, including areas to which coronary artery disease pain is referred (24, 67). The attacks are precipitated by an emotional disturbance and are relieved by expelling gas or feces (spontaneously or enema-induced), providing the pressure in the splenic flexure is thereby decreased.

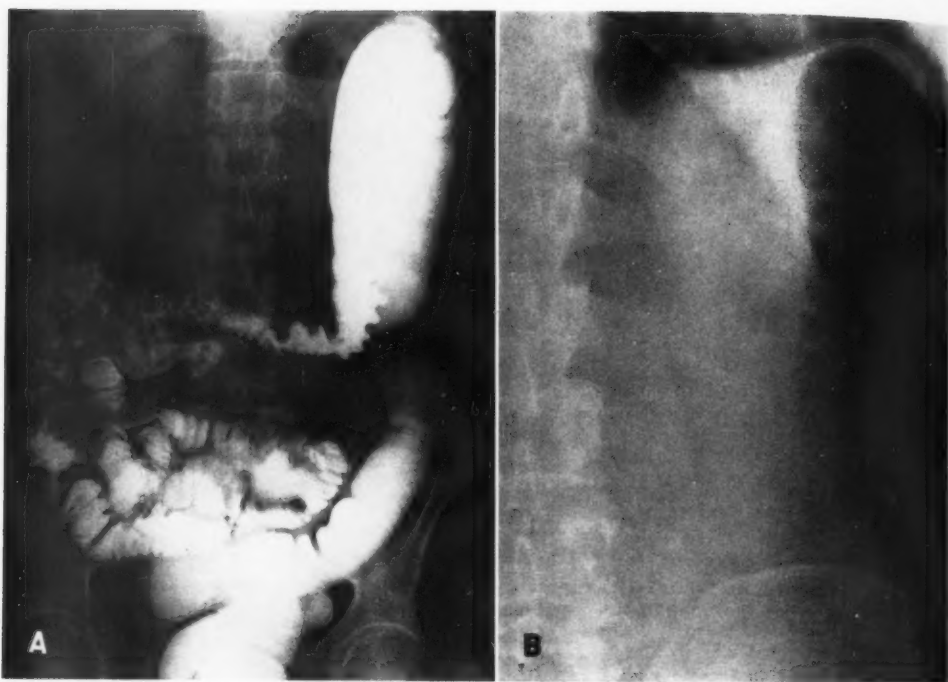


Fig. 12. A. Distention of splenic flexure and descending colon. The proximal transverse colon is contracted and irritable.

B. Splenic flexure of colon outlined by gas. The spindle-shaped narrowing of the proximal descending colon leads to a spastic segment of descending colon just above the crest of the ileum.

During attacks, spasm is present in the descending colon (Fig. 12, B) which cannot be overcome by the powerful forward propulsive forces in the transverse colon (Fig. 12, A); consequently the splenic flexure distends. The pain can be reproduced by air inflation of a balloon in the splenic flexure (24).

Occasionally patients with *severe pain and manifestations of colonic obstruction due to prolonged localized spasm* are encountered. The area of spasm cannot be filled out during barium enema and a malignant neoplasm is suspected. Colp (18) reported 5 cases of obstruction of the large intestine in which preoperatively a malignant condition was diagnosed but which subsequently proved to be due to muscular spasm.

Painful cramps originating on the basis of small intestinal hypermotility may arise when the entire colon is hypertonic or in spasm (Fig. 13).

(b) *Constipation Without Pain*: Mild episodes of painless constipation are not infrequently associated with periods of prolonged travel. In some persons subjected to continued stress, periods of constipation lasting as long as nine to ten days may occur without significant pain (Fig. 14). Such patients, however, may experience an enlargement in the right side of the abdomen after meals, often requiring the loosening of tight belts or garments (Fig. 15).

(c) *Diarrhea With Pain*: Diarrhea on the basis of irritable colon, sometimes called mucous colitis, is frequently associated with cramps along the course of the colon. The stools are loose and contain mucus but no blood unless bleeding occurs from a hemorrhoid, fissure, or polyp. Some patients experience an urge to defecate after meals. In such instances, small intestinal as well as gastric hypermotility is usually associated with hypermotility

in the large intestine (Fig. 16). The diarrhea as a rule does not occur at night, as sleep depresses colonic motor activity (80). This is often a useful clinical point in differentiating functional diarrhea from that due to ulcerative colitis. Diarrhea due to irritability of the colon can occur at night, however, if the patient is awake and emotionally disturbed.



Fig. 13. Marked spasm of transverse colon and hypertonicity of descending colon in patient with small-intestinal hypermotility. She had had a subtotal gastric resection for duodenal ulcer previously. Eating was usually associated with borborygmi and severe abdominal cramps, often necessitating interruption of a meal.

(d) *Diarrhea Without Pain:* Diarrhea on the basis of irritable colon is more frequently associated with abdominal cramps than not. In the absence of pain there may be a sensation in the rectum inciting a desire to expel its contents when the colon discharges material into it.

(e) *Alternating Constipation and Diarrhea:* Some patients experience periods of constipation alternating with diarrhea. Either symptom may be associated with abdominal discomfort as previously described, and the roentgen pictures are similar. Studies made on such patients by Grace (44) indicated that episodes of

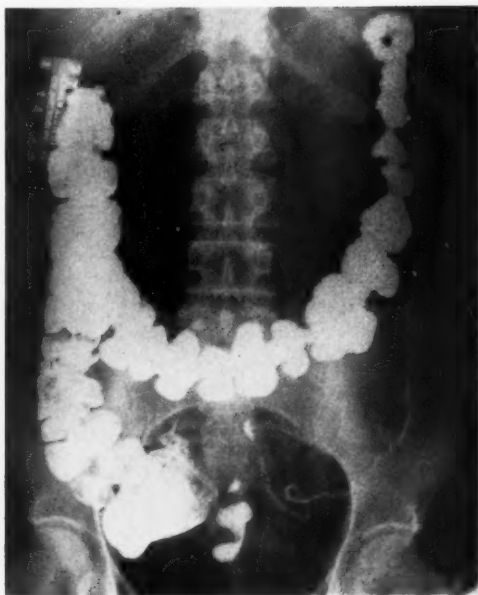


Fig. 14. Severe spasm of descending colon in a patient with painless constipation.

constipation coincided with periods of sadness and dejection in which the patient continued to strive and work in the face of a hopeless attitude. Diarrhea, on the other hand, occurred during situations to which the subjects reacted with fear, anxiety, guilt, and resentment. The general attitude at such times was one of being overwhelmed and unable to fight back. The significance of these striking temporal coincidences was reinforced by short-term experiments in which stress was applied by a discussion of personal conflicts while observations on colonic activity were being recorded. During sadness and dejection the colon became slack, elongated, and hypomotile. During experimentally induced periods of anxiety, guilt, and resentment, the colon became contracted, shortened, and hypermotile.

2. *Hypofunction of Colon:* Dilatation and decreased motor activity of the colon (Fig. 17) on a psychogenic basis leading to retention of feces is not infrequently encountered and has to be differentiated from megacolon due to congenital absence of ganglion cells from the plexuses in the

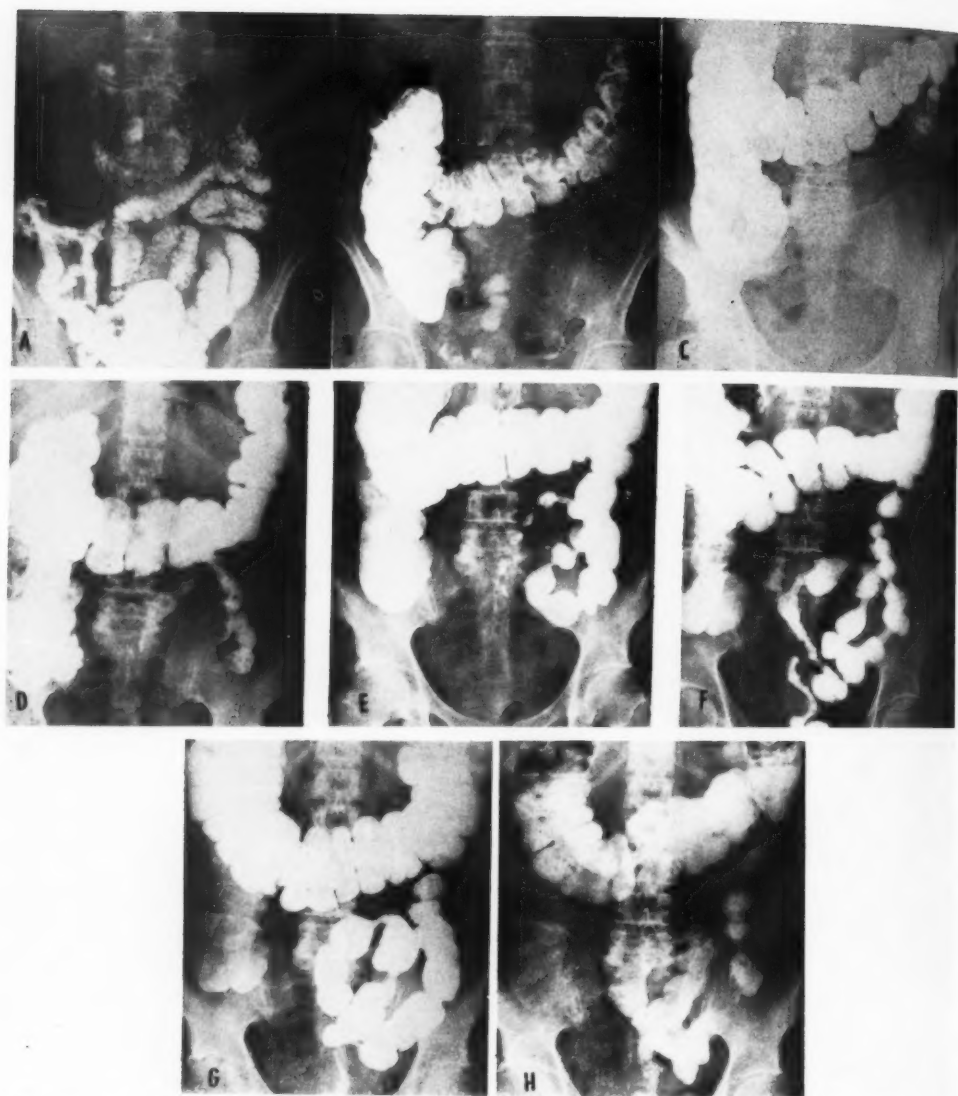


Fig. 15. Progress of head of column of barium meal in patient with "painless" spastic constipation in whom a regular barium enema was negative for evidence of organic disease.

- A. Day 1. Appearance about two hours after ingestion of barium meal. The head of the column is in the distal ileum.
- B. Day 1. Seven hours after ingestion of barium meal. The head of the column is in the proximal splenic flexure.
- C. Day 2. Very little progress of head of column of barium twenty-four hours after ingestion of the barium meal. The head of the column is in the proximal descending colon.
- D. Day 3. Very slight progress of the head of the barium column. The descending colon is hypertonic.
- E. Day 4. The head of the column is approaching the sigmoid.
- F. Day 5. Barium has reached the rectum. Two stools passed following laxative prescribed the evening before showed no recognizable barium.
- G. Day 6. Patient passed a stool containing barium. Barium density is less marked in the cecum. Laxative prescribed the evening before.
- H. Day 8. Barium still present in the colon. The descending colon continues to be hypertonic.

lower sigmoid and/or rectum (Hirschsprung's disease). A great deal of confusion exists as to etiology and result of therapy for megacolon, primarily because these two types are not always differentiated.

In psychogenic megacolon the dilatation of the colon begins directly above the anus. There is no spasticity of the rectum or rectosigmoid, which instead are usually quite large and full of feces. Onset occurs during the second year of life or later. This type of megacolon appears to be due to an overactivity of the sympathetic and/or an underactivity of the parasympathetic nervous system. The process usually begins in the distal colon and can remain localized or may extend throughout the entire length of this part of the bowel. An aganglionic segment is not demonstrable.

The disorder is not infrequently encountered in infants and children whose parents manifest great concern about the child's bowel movements. Frequently there has been coercive bowel training (35). The outstanding symptom is constipation. In addition there may be fecal soiling. The possibility of a megacolon of this type may be suspected when large subphrenic gas bubbles are noted on chest roentgenograms. A barium enema will show a greatly dilated colon (100). Occasionally a large fecalith in the rectum may be revealed (Fig. 18).

In contrast, congenital megacolon or Hirschsprung's disease is currently believed to be caused by a functionally deficient segment of rectum or rectosigmoid resulting from a congenital absence of the ganglion cells from Auerbach's and Meissner's plexuses in the lower sigmoid and/or rectum. Constipation without fecal soiling occurs at birth or during the first few weeks of life. A spastic segment of rectum or rectosigmoid can be demonstrated by Neuhauser's fluoroscopic technique. Removal of the aganglionic segment is said to be the rational treatment of Hirschsprung's disease and has given reasonable results.

Megacolon may also occur secondary to



Fig. 16. Appearance of colon about fifteen minutes after ingestion of barium meal in a patient having 16 to 20 stools per day. The colon is irritable and transporting its content with great rapidity.

retroperitoneal cancer, particularly carcinoma of the pancreas. In such cases, in addition to anorexia and loss of weight, a marked delay in evacuation of barium, sometimes for as long as two to eight weeks, may be the only clue to the existence of a pancreatic growth. Enlargement of the colon has also been reported in association with hypothyroidism (7) and secondary to vitamin B<sub>1</sub> deficiency (29). Injury to the intramural plexuses by the parasite *Trypanosoma cruzi* has been claimed to be responsible in some instances (56) of American trypanosomiasis.

Motor as well as propulsive activity may be induced in megacolon by the administration of acetyl-beta-methylcholine (60), Urecholine, or Doryl (45), in adequate dosage.

#### SUMMARY

1. Functional motor disturbances of the gastrointestinal tract which are responsible for symptoms can be readily recognized by the radiologist on the basis of fluoroscopic examination and inspection of



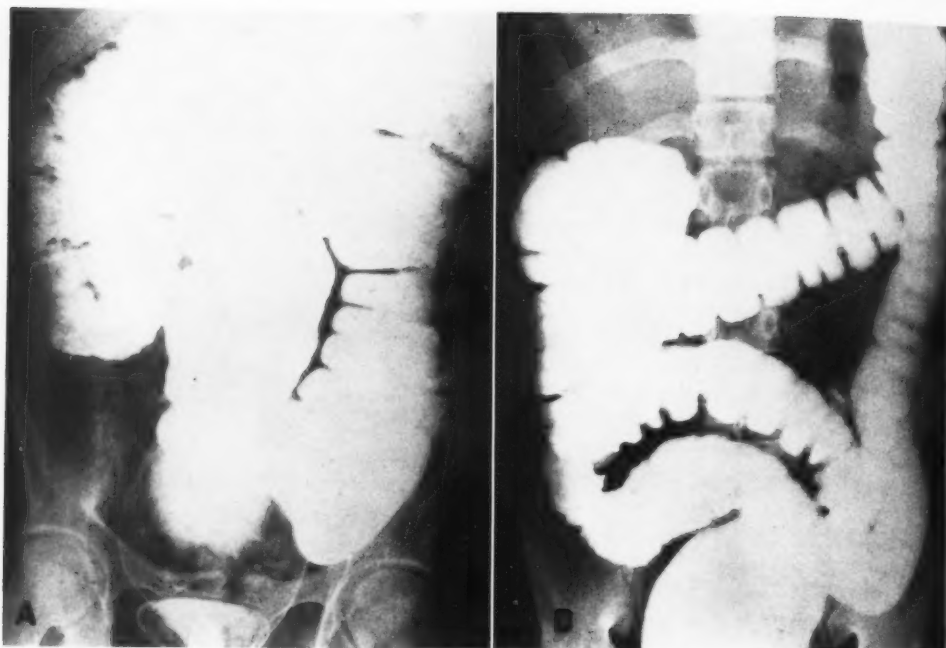


Fig. 17. A. Appearance of colon following barium enema in a 21-year-old patient with psychogenic megacolon who had not had a spontaneous bowel movement since childhood. No spastic segment in the rectum or sigmoid is seen, as is characteristic of Hirschsprung's disease.

B. Appearance of colon while on Urecholine; the patient having daily bowel movements for the first time in his life.



Fig. 18. Fecalith in rectum of patient with atonic colon on a psychogenic basis. At laparotomy, the fecalith was found to consist of matted vegetable fibers and resembled a bird's nest.

films made during the course of clinical manifestations.

2. The motor abnormalities occur in patients subjected to frustrating, stressful life situations. In general—though not invariably—anger, resentment, and hostility cause motor disturbances similar to those following excitation of the parasympathetic division of the autonomic nervous system, while fear and sadness mimic the actions of the sympathetic system.

The functional disturbances which appear to be due to predominantly parasympathetic influences are esophagospasm, gastric hypermotility, duodenal spasm and hypermotility, and spastic disorders of the small and large intestine. Those which appear to be due to sympathetic hyperactivity or parasympathetic underactivity include achalasia of the esophagus, gastric retention in the absence of obstruction, megaduodenum, and hypoactive states of the colon, including "psychogenic" megacolon.

3. Management consists of an attempt to help the patient solve his emotional problems, as well as the administration of drugs to correct the abnormal physiological state. Urecholine, a parasympathomimetic agent, is administered to correct hypoactive states, and anticholinergics and sedatives to correct hyperactive states.

4. Anticholinergic drugs are of little help in controlling marked spastic states of the descending colon. Demerol, by injection, will usually relax the left side of the colon but its repeated use may lead to addiction.

5. Somatic changes may occur when functional disturbances persist. For example, achalasia may lead to megaesophagus, and high intraluminal pressures in the irritable colon to diverticulosis and its various complications.

6. It must be emphasized that before one ascribes symptoms to functional motor disturbances, responsible organic disease should always be carefully ruled out.

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## SUMMARIO IN INTERLINGUA

## Disturbationes Functional del Vias Gastrointestinal

Disturbationes motori functional del vias gastrointestinal que es responsabile pro symptomatas pote esser recognoscite prestemente per le radiologo super le base del examine fluoroscopic e del inspection del radiogrammas facite durante le curso del manifestationes clinic.

Le anormalitates motori occurre in patientes subicite a eventos frustratori e stressose in lor vitas. A generalmente parlar—ben que non invariabilmente—vexation, resentimento, e hostilitate causa disturbationes motori simile a illos observate post excitation del division parasymphatic del systema nervose autonome, durante que timor e tristessa simula le actiones del systema nervose symphatic.

Le disturbationes functional que pare esser causate predominantemente per influentias parasymphatic es esophago-spasmo, hypermotilitate gastric, spasmo e hypermotilitate duodenal, e disordines spastic del intestinos tenue e crasse. Le disturbationes functional que pare esser causate per hyperactivitate symphatic include achalasia del esophago, retention gastric in le absentia de obstruction, megaduodeno, e statos de hypo-activitate colonic, incluse megacolon "psychogene."

Le tractamento consiste de tentativas de adjutar le patiente in su problemas emotional e in le administration de drogas capace a corrigir le stato physiologic.



## Fat Absorption from the Human Gastrointestinal Tract in Patients Undergoing Radiation Therapy<sup>1</sup>

R. J. REEVES, A. P. SANDERS, J. K. ISLEY, K. W. SHARPE, and G. J. BAYLIN

THE EFFECT OF ionizing radiation on the gastrointestinal tract was first noted by Walsh in 1897 (1). The circumstances under which the irradiation was given and the amount are unrecorded. Since that time, many studies as to the effect of radiation on the digestive tract have been carried out. These have been directed toward a morbid anatomical evaluation or a physiological evaluation, or both.

Excellent studies of the anatomical changes in the small bowel after irradiation in varying amounts may be found in papers by Warren (2, 3), Martin (4), and Senn (5). Their observations have been substantiated by many other workers. The changes have consisted primarily of a loss of the intestinal epithelium, beginning with that in the crypts and progressing to the villi. Ulcerations then appear, extending through the submucosa and sometimes into the serosa. The extent of these lesions and the rapidity with which the process develops depend to a large extent upon the tissue dose received by the area. It has also been found to vary with the experimental animals used (6, 7).

The other approach to the study of small bowel damage has been from a functional standpoint. As two of the main functions of the small bowel are motility and absorption, the study may be oriented toward one or both of these. Wallace (8), in 1941, studied a series of our patients undergoing deep x-ray therapy to the pelvis. He found a decreased motility and segmentation of barium in the ileum. He noted also some apparent loss of ileal mucosal pattern on the barium studies. Conard (9) made an extensive study of the motility of the small bowel in rats. He reported a transient increase

after irradiation, followed by a generalized slowing with a gradual return to normal on the third or fourth day. Greenfield (10) observed delayed gastric emptying time in rats after irradiation.

A second approach to this problem from the physiological aspect is that offered by a study of the absorptive mechanism. Greenfield, working with white rats, described a decrease in the ability of the small bowel to absorb Evans blue dye after irradiation. Buchwald (11) and Moss (12) found a decreased intestinal absorption of carbohydrates, in the form of glucose, mannose, fructose, and arabinose, following irradiation to the exteriorized small bowel in the rat.

In 1924 Martin and Rogers (13) described a decrease in fat absorption from the small bowel in irradiated dogs. They carried out their study by staining the intestinal epithelium for fat, after a fatty meal had been administered to the animal. No fat droplets were found within the mucosa, whereas normally they are present in abundance. In 1951 a study of the absorption of fat from the irradiated small bowel of mice was carried out by the use of methyl oleate, with spectrophotometrically active octadecadienoate as a tracer (14). The mice were given 600 to 700 r total body irradiation. There was some increase in the total fat loss in the feces, but this was believed to have an endogenous origin, as it was found to occur in animals while on a fat-free diet. It was concluded that there was no evidence of failure of the small bowel to absorb fat in the irradiated mice.

In 1955, Baylin *et al.* (15) reported a simple technic for evaluating the intestinal ability to absorb fat by the use of iodine-131-labeled glycerol trioleate. The ma-

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## FAT ABSORPTION STUDIES ON DEEP X-RAY THERAPY PATIENTS

• - Normal Absorption ; x - Decreased Absorption

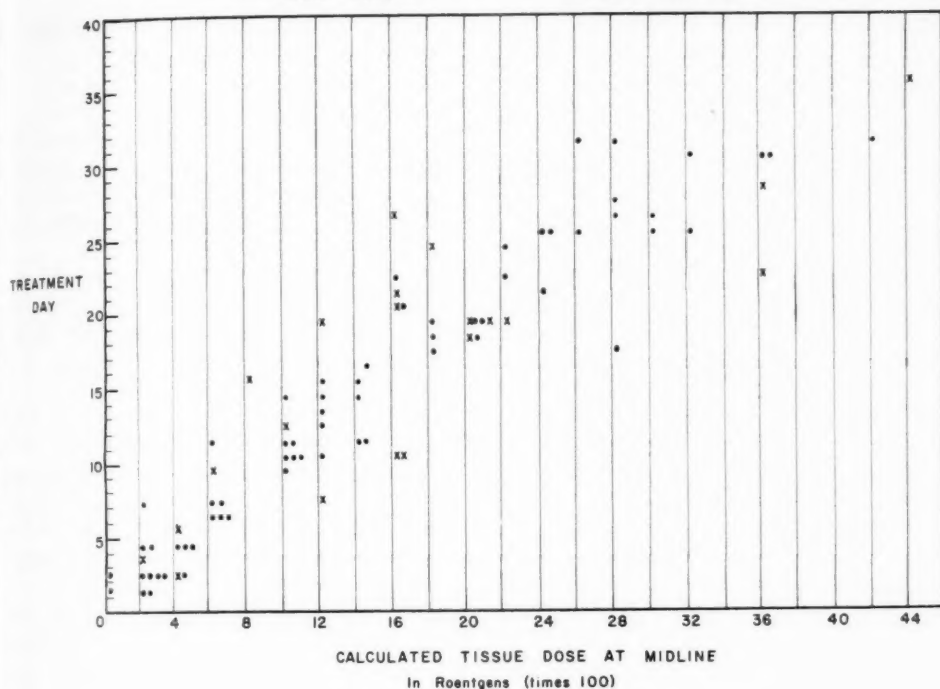


Figure 1

terial was administered orally and blood levels were subsequently obtained. Sanders *et al.* (16) later described a procedure for determining the fat absorption from the bowel by radioanalysis of the feces, with the same material. These procedures have been subsequently modified for use with oleic acid (17).

## PROCEDURE AND MATERIALS

The material for this study consisted of 29 patients who entered the x-ray therapy department at Duke University Hospital for treatment of carcinoma of the cervix. All ambulatory patients were studied. A control fat-absorption study after the technic of Baylin (15) and fecal analysis as described by Sanders (16) were carried out prior to the institution of therapy in 23 of these patients. In the remaining 6, oleic acid absorption studies were done.

The patients were started upon a course

of x-ray therapy through two anterior and two posterior opposing ports. The size of the portals varied from  $8 \times 12$  to  $12 \times 15$  cm., and the focal skin distance from 50 to 70 cm. The beam, 200 kvcp, had a half-value layer of 1.65 mm. of copper. Treatment was given at the rate of 200 r daily through two ports.

According to a predetermined schedule, fat absorption studies were done on all patients at varying times during the course of therapy. These procedures consisted of blood or fecal analyses or both. They were carried out in a manner identical to the control studies. A total of 373 blood radioactive determinations and 125 fecal determinations were obtained on these 29 patients.

## RESULTS

Figure 1 shows the observations on the 10 patients in whom decreased absorp-

tion of the glycerol trioleate was demonstrated either by blood analysis or by fecal analysis. The comparison as to the number of treatment days may be noted. The table also shows the estimated tissue dosage to the midline at the time the absorption study was done.

Of the 6 patients studied with oleic acid, 3 were found to show a decreased absorption. This change was noted in the fecal analyses only. The abnormalities were present on tests done on the fifth and sixteenth treatment days in 1 case and on the twelfth and sixteenth days in the other 2. Tumor dosages at the midline ranged from 945 to 3,100 r. Additional tests on these patients showed a return to normal before the end of the treatment series in a fashion similar to that with glycerol trioleate.

#### DISCUSSION

As noted above, there have been studies on animals prior to this, suggesting that the small bowel undergoes a loss of its absorbing ability after irradiation damage. This study serves to confirm these earlier observations and to point out that this phenomenon may now be demonstrated in human beings undergoing conventional x-ray therapy in which a normal small bowel, primarily ileum, receives irradiation.

The patients may be placed in three primary groups on analysis.

1. Those patients whose blood and fecal analyses remained within normal limits. None of these patients experienced clinical diarrhea.

2. Those whose blood values decreased but remained within normal range. Some of these patients showed an increase in fat loss in the stool to definite abnormal levels and some experienced mild diarrhea. The number of cases is insufficient for statistical evaluation.

3. Those patients who showed a definite decrease to below normal levels of blood radioactivity and high fecal fat values. In these cases definite clinical diarrhea developed.

From the above findings, it would appear

that the fecal analysis is the more sensitive of the two test procedures. It might also be the most treacherous, however, as urine contamination may easily give false positive results. It might further be pointed out that many of the blood values, although remaining within normal limits, decrease somewhat after irradiation to the bowel.

The series of patients studied with oleic acid is not large; 3, however, definitely showed an abnormality of absorption. This was present, as one would expect it to be, when the defect lay in the absorbing mucosa and not within the digestive mechanism.

#### SUMMARY AND CONCLUSIONS

Functional impairment of the human bowel undergoing irradiation may be quite easily demonstrated in some cases. A study of this aspect of radiation damage was made from the point of view of fat and fatty acid absorption. Thirteen of 29 patients undergoing x-ray therapy involving the lower abdomen were found to exhibit transient decreased fat or fatty acid absorption during the course of irradiation.

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## SUMMARIO IN INTERLINGUA

## Le Absorption de Grassia ab le Vias Gastrointestinal in Patientes Subjicite a Therapia Irradiational

In certe casos il es facile demonstrar effectos dysfunctional in intestinos human que es subjicite a irradiation. Un studio de iste aspecto del injurias radiatori esseva interprendite ab le puncto de vista del absorption de grassia e acidos grasse.

Esseva trovate que 13 ex 29 patientes tractate per roentgeno-therapia afficiente le abdomine inferior exhibiva transiente reductiones del absorption de grassia o de acidos grasse durante le curso del irradiation.



# Significance of Calcification of the Wall of the Left Atrium

## Report of Two Cases<sup>1</sup>

PAUL S. MAHONEY, M.D., and BERNARD J. O'LOUGHLIN, M.D., Ph.D.

CALCIFICATION of the wall of the left atrium was first reported by Shanks, Kerley, and Twining in 1938 (6). Since that time, only 31 cases have been reported. Although intramural calcification of the left atrium is primarily a radiological diagnosis, this concept has not been presented to the readers of this journal. It is believed that this lesion is more common than has been manifested by the published reports. In adding 2 new cases to the 31 reported in the literature, the importance of recognizing calcifications of the left atrium will be stressed, particularly in those cases in which some surgical procedure upon the heart is contemplated.

Calcification of the left atrium is found in patients who have suffered from extensive rheumatic carditis and long standing valvular disease. It is believed that the calcification of the wall of the left atrium represents the site of the carditis. Many of these patients suffer from both mitral stenosis and insufficiency and most of them have involvement of other valves as well as the mitral valve.

The pathological findings are chiefly subendocardial plaque formation, endocardial fibrosis, connective-tissue hyperplasia, and Aschoff nodule formation. It appears that the site of predilection for the endocarditis is on the posterior wall of the atrium above the mitral valve. The extent of the auricular lesion is usually related to the severity of the valvular disease.

Ruskin and Samuel (11) have reviewed and summarized the cases of this disease which have been reported in the literature and have added two cases of their own. They find that the average age of the patients with calcification of the wall of the left atrium is fifty-one years. The

average length of time which these people have suffered from rheumatic heart disease has been twenty-nine years. Most of the patients have had symptoms for seventeen years or more. A calculation of the concomitant complications in a person with extensive calcification of the left atrium revealed the incidence of auricular fibrillation to be ten years. Congestive heart failure occurred in 80 per cent, and the average duration of congestive failure was eleven years. Hypertension was found in 10 per cent of the patients. The average age at death was fifty-three years.

The diagnosis of calcification of the left atrium frequently can be made on a plain chest film. Slightly overexposed Bucky films of the chest, body-section studies through the left atrium, or roentgen cinematography may be needed to confirm the diagnosis. Soloff, Zatuchni, and Fisher (12) stress the importance of planigraphy and report 2 cases of calcification of the left atrial wall discovered in this way that were totally unsuspected in routine projections of the chest. Moderate amounts of calcium can always be identified on chest films of good technical quality, although the anatomical site and pathological process may not be as readily apparent.

The differential diagnosis of atrial calcification should include other major anatomical structures in the heart which may calcify, such as coronary arteries, ventricular walls (aneurysms), cardiac valves, and the pericardium. The most important and yet the most difficult differentiation, however, lies between a partially calcified mural thrombus and a calcified left atrial wall. Intramural calcification is usually linear, nonlaminated, and marginal in distribution. A calcified mural

<sup>1</sup> From the Department of Radiology, University of California School of Medicine, Los Angeles, Calif. Accepted for publication in November 1958.

thrombus, on the other hand, is usually laminated and nonlinear. Other cardiac calcifications are more easily differentiated. Calcified coronary arteries are visualized as thin parallel lines, seen best at fluoroscopy. They occupy a characteristic position on the roentgenogram and are usually seen in the anterior descending or circumflex branches. The few ventricular aneurysms which do calcify are usually extensively calcified and are most often located at the apex of the left ventricle. Valvular calcifications of the mitral and aortic valves can easily be distinguished fluoroscopically, being more central in location and exhibiting a characteristic dancing motion. Pericardial calcifications are usually seen at the periphery of the heart. They are identified by the relative lack of cardiac pulsations adjacent to them and are best seen in the various oblique projections at fluoroscopy. Calcified cardiac tumors and calcified pericardial cysts are extremely rare and often can be differentiated with the aid of the fluoroscope. Calcified hilar lymph nodes and calcified costal cartilage can be excluded in the various oblique projections. Other possible causes of endocardial calcification may be vitamin D intoxication or some such disturbance in the calcium metabolism as idiopathic hypercalcemia. These metabolic changes may be clarified by various laboratory examinations and in this group calcification is often observed in other areas of the body.

If calcification of the wall of the left atrium is identified prior to mitral valvulotomy, the patient should be reappraised in the light of this finding (since the lesion may then be considered inoperable), which may prove to be an invaluable aid to the surgeon, who elects to proceed with the operation in the face of the added risk. Instead of doing his valvulotomy *via* the usual route, through the left atrial appendage, he may choose to go through the pulmonary vein. This change in approach to the mitral valve tends to minimize the danger of breaking the brittle calcified auricular wall into fragments. Such small



Fig. 1. Case I. Plain roentgenogram showing linear marginal calcification of left atrial appendage and left atrial wall along the right border of the heart. The typical mitral configuration of the heart is well demonstrated.

calcific fragments may enter the circulation, causing peripheral or central nervous system emboli. O'Farrell (10) reports a case in which the surgeon was unable to complete the mitral valvulotomy because of dense calcification of the left atrium. These characteristic findings were overlooked on the preoperative roentgenogram, but in retrospect the calcific outline of the left atrium could be seen clearly. Other surgeons report extensive and uncontrollable bleeding upon penetrating the calcified left atrial appendage in the process of mitral valvulotomy. (Unfortunately for the surgeon, the left auricular wall is the part of the atrium most frequently involved, but fortunately for the radiologist the heaviest deposits of calcium are found here in an anatomic area whose ear-shaped appearance is most easily recognized.)

#### CASE REPORTS

CASE I (Figs. 1 and 2): W. O., a 36-year-old thin white woman, was admitted to the hospital in 1950, complaining of progressive shortness of breath, and exertional dyspnea. She denied having



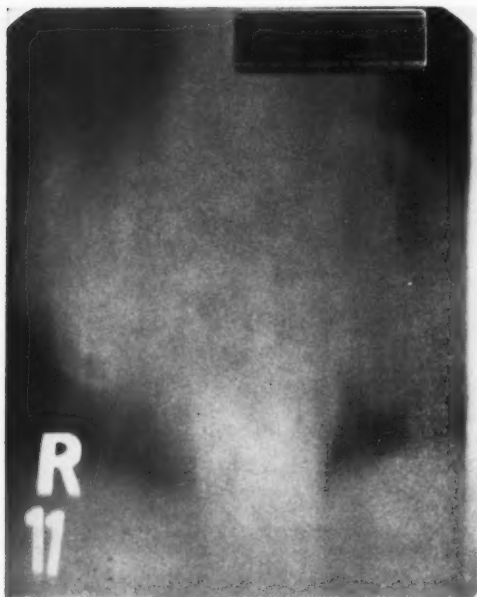


Fig. 2. Case I. Planigram showing extensive calcification along the right border of the left atrium and the left atrial appendage.

had rheumatic fever, joint pains, rash, or epistaxis. A diagnosis of rheumatic heart disease was made in 1931 and she had been receiving digitalis for fifteen years. Pedal edema developed ten years prior to admission and auricular fibrillation nine years prior to admission.

**Physical Examination:** Blood pressure 124/85; pulse irregular and slow; apical impulse in the anterior axillary line of the 6th intercostal space; T2 split and louder than A2. A diastolic and pre-systolic murmur was heard at the apex, with a diastolic thrill palpable at the apex. No systolic murmur was audible. The liver was palpable one and a half finger breadths below the right costal margin, and there was pitting edema of both feet.

The electrocardiogram revealed a slight right axis deviation, auricular fibrillation, and digitalis effect.

Fluoroscopy demonstrated cardiomegaly and an extremely large left atrium. Definite calcification was noted in the left atrial wall and the left atrial appendage but none in the mitral valve. The esophagus was displaced posteriorly and to the right by the huge left atrium. The pulmonary artery segment was prominent. The lung fields were congested. A confirmatory chest film and planigram are shown in Figs. 1 and 2.

Operation was undertaken despite knowledge of the extensive calcification of the left atrial wall, the surgeon electing to perform the valvulotomy through the left atrial appendage. Extensive bleeding and difficult hemostasis prolonged the operation, and the patient was returned to the ward in a

precarious condition. Recovery was otherwise normal and she was discharged on the seventeenth postoperative day and is alive seven years following surgery. At the present time her symptoms are controlled on a maintenance dose of digitalis.

**CASE II (Fig. 3):** A. P., a 58-year-old thin white woman, was admitted to the hospital complaining of shortness of breath and ankle edema. She had rheumatic heart disease at the age of fourteen. Dyspnea, ascites, and weight loss had their onset two years prior to admission. Dyspnea and orthopnea were progressive in spite of intensive medical management.



Fig. 3. Case II. Lateral view demonstrating calcification of the superior border of an enlarged left atrium which is displacing the esophagus posteriorly.

**Physical Examination:** Blood pressure 108/70; venous pressure 155 mm. Hg; circulation time 36 seconds. The neck veins were distended and there was 3+ pedal edema. Signs of bilateral hydrothorax were present, and there were moist râles in both upper lung fields. The heart was moderately enlarged, with a Grade II diastolic murmur, heard best at the apex. The liver extended four finger breadths below the right costal margin.

A chest roentgenogram revealed concentric cardiomegaly with characteristic calcification of the left atrial wall and bilateral pleural effusions. The electrocardiogram showed auricular fibrillation, right ventricular hypertrophy, and digitalis effect. Vigorous attempts were made to relieve the patient of excessive body fluid, but, in spite of intensive medical therapy and numerous thoracenteses, her condition became progressively worse and she expired on the twentieth hospital day.

**Postmortem Report:** Chronic rheumatic mitral endocarditis with stenosis and insufficiency; a large mural thrombus in the left atrium; extensive calcification of the left atrial wall; also bilateral pulmonary congestion, edema, and hydrothorax.

## SUMMARY

Calcification of the wall of the left atrium is a complication of long standing rheumatic heart disease. It appears to be associated with the more severe cases, with extensive carditis and valvular disease, and is of both pathological and surgical significance. As a general rule it is an unfavorable prognostic sign.

Two cases are added to the 31 previously reported in the literature. The roentgen appearance is characteristic, and the diagnosis can frequently be made from the plain postero-anterior chest film.

**NOTE:** Since the acceptance of this contribution for publication, there has appeared a paper, *Left Atrial Calcification*, by Vickers, Kincaid, Ellis, and Bruwer, in *RADIOLOGY* 72: 569-574, April 1959.

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## SUMMARIO IN INTERLINGUA

## Le Signification de Calcification del Pariete Sinistro-Atrial: Duo Casos

Calcification del pariete sinistro-atrial es un complication de rheumatic morbo cardiac de longe duration. Il pare que illo es associate con le casos plus sever, con extense carditis e morbo valvular, e es de signification tanto pathologic como etiam chirurgic. A generalmente parlar,

illo es disfavorabile como criterio prognostic.

Es addite duo nove casos al 31 jam reportate in le litteratura. Le diagnose pote frequentemente esser facite super le base del regular exposition thoracic postero-anterior.

## Extraosseous Infiltration in Multiple Myeloma<sup>1</sup>

JAMES A. GILROY, M.D.,<sup>2</sup> and ANDREW B. ADAMS, M.D.

IN THE BIZARRE disease multiple myeloma, the possibility of soft-tissue lesions is often overlooked. Up to 1950, a total of 182 cases of extraosseous myeloma had been reported (1), mostly in the nonradiologic literature. This figure does not provide an indication of actual incidence, however, since many cases never come to autopsy. In several series of cases of multiple myeloma in the literature, plasma cell infiltration of soft tissue was said to be present in 50 to 73 per cent of patients (1-3). For the most part such involvement was due to osseous lesions that had broken through bone and extended into contiguous structures.

The following case is noteworthy because the patient had extensive myelomatous involvement throughout the body but only a single bone lesion, a rounded osteolytic area in the skull. In addition, there was a pulmonary lesion that simulated a bronchogenic carcinoma radiographically, and the case was further complicated by the presence of a papillary carcinoma of the bladder.

### CASE REPORT

A 54-year-old white man had been in excellent health until December 1955, when hematuria was discovered and he was found to be anemic. Cystoscopic studies at another hospital revealed a polypoid lesion in the bladder. The patient was transferred immediately to Strong Memorial Hospital for surgery.

Except for pallor, the physical findings were unrevealing. Intravenous pyelograms and barium studies of the colon were interpreted as normal. An anteroposterior radiograph of the chest (Fig. 1) showed nodularity of the right hilus and unequivocal widening of the mediastinum, which were considered evidence of probable bronchogenic carcinoma with mediastinal metastases. Because of these findings, a radiographic survey for metastases was carried out. Only mild generalized osteoporosis and a single round osteolytic lesion in the skull (Fig. 2) were discovered.



Fig. 1. Roentgenogram of chest obtained on admission: nodularity of right hilus and mediastinal widening.

Aspiration of the sternal bone marrow revealed that 20 per cent of the nucleated elements consisted of plasma cells. Bence-Jones protein was not present in the urine. Cystoscopy was again performed, and a biopsy specimen of the bladder tumor obtained. The pathologist's diagnosis was papillary carcinoma.

The following diagnoses were made: papillary carcinoma of the bladder, multiple myeloma, and possible bronchogenic carcinoma of the right lung with mediastinal metastases. In connection with this last, the possibility of a lymphomatous process, *e.g.*, Hodgkin's disease or lymphosarcoma, was also considered. This was suggested on the basis of the radiographic findings alone.

While the patient was being prepared for surgery of the bladder lesion, extreme difficulty was encountered in cross-matching blood. This was attributed to autoagglutination. When cross-matching was accomplished, the tumor was resected. The operation was well tolerated.

Following discharge from the hospital, the patient did quite well for a time and then began to experience intermittent fever and profuse night sweats. He was readmitted June 18, 1956. There were no significant physical findings, and radiographs of the

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Fig. 2. Roentgenograms of skull, showing single round osteolytic lesion.

chest showed no change from the previous examination. A scalene biopsy was negative. Pathologic study of tissue removed from the walls of the bronchi during bronchoscopy, however, revealed widespread invasion of the submucosa by plasma cells. It was decided that radiation therapy was indicated, and a total of 3,000 r was administered to the mediastinum through anterior oblique ports and a single posterior port over a period of eighteen days. The factors were 280 kv, h.v.l. 1.0 mm. Cu. Radiographs made immediately following completion of therapy showed no change in the width of the mediastinum.

The patient was again discharged but was readmitted thirteen days later with symptoms of mild esophagitis. An anteroposterior radiograph of the chest made at that time (Fig. 3) revealed a definite decrease in width of the mediastinum. Following this the patient felt fairly well until October 1956, after which he deteriorated rapidly and died.

**Postmortem Examination. Gross Findings:** A large firm mass, pale gray in color, was present in the superior mediastinum (Fig. 4). It extended around the trachea to the right and posteriorly, measuring 10 cm. in length and 5 cm. in width. There was no evidence of tracheal obstruction nor of attachment of the mass to the thoracic skeleton. A rounded mass of similar gray tissue, 3 cm. in diameter, was present in the right hilus.

A round lesion, 2 cm. in diameter, located in the right frontoparietal region of the skull had the consistency of soft cartilage and was covered by an egg-shell-like layer of bone. The dura mater was not involved.

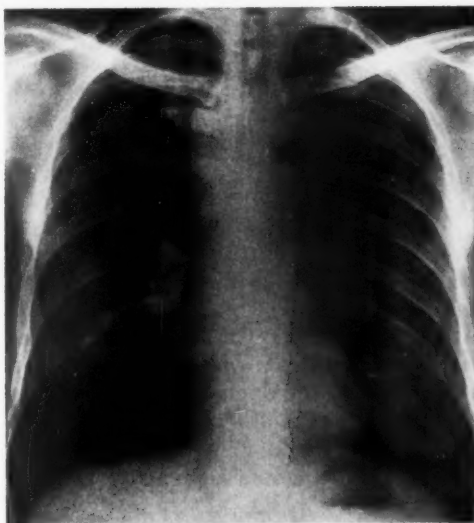


Fig. 3. Roentgenogram of chest, showing definite decrease in mediastinal widening following radiotherapy.

The lungs were firm. Their cut surfaces were reddish gray in appearance and heavily streaked with fibrotic bands. Crepitation was diminished.

The heart, spleen, pancreas, liver, adrenal glands, and alimentary organs were unremarkable.

**Microscopic Findings:** The mediastinal lesion was composed of large masses of plasma cells in a stroma of fibrous connective tissue. The cells

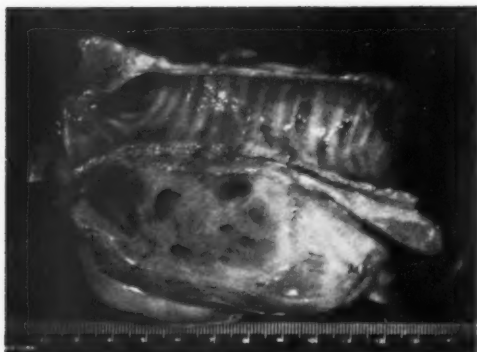


Fig. 4. Mediastinal mass; autopsy specimen.

were large and exhibited numerous mitotic figures. There was no apparent involvement of the mediastinal lymph nodes. The right hilar mass consisted of lymph nodes in which the lymphatic tissue had been almost completely replaced by plasma cells. Only the nodal sinuses had been preserved. Sections of the cranial lesion revealed densely packed plasma cells in a fine reticular stroma.

The lungs presented a uniform picture of fibrosis, congestion and consolidation, with patches of atelectasis and emphysema. Exudate indicative of acute inflammation was absent.

The spleen exhibited many plasma cells scattered throughout the red pulp, and plasma cells were the major cellular component in the bone marrow generally.

#### DISCUSSION

The origin of extraosseous plasma-cell tumors in multiple myeloma has been and still is in doubt. In their excellent review Geschickter and Copeland (4) found a sufficient number of cases in which plasma cells were present within the lumen of blood vessels to conclude that metastases by way of the blood stream were common.

Perhaps more dispute has centered on the mode of metastasis in myeloma than on any other point. Is it a disease of multifocal origin or does it begin as a solitary lesion with subsequent metastases? If the latter is true, why then are the metastases so prone to appear in most cases only in bone?

At this time, these questions are by no means answered. Since the origin of the plasma cells themselves is still in dispute, this is even more understandable. Maxi-

mow, in his original work in 1920, produced plasma cells in culture by explants of lymphoid tissue. Since then, a theory has been widely accepted that they develop from reticular cells.

Plasma cells have been found in almost every organ of the body in cases of multiple myeloma. Most commonly involved, exclusive of bone, are lymph nodes (12), liver (2), spleen (7), and kidneys (8). Bizarre extraosseous involvement such as massive retroperitoneal myeloma has been reported (2). In several reported cases, as in ours, the soft-tissue lesions have been intrathoracic. These have included intrapulmonary disease (9, 11), a tumor projecting from the pleura (10), and mediastinal involvement (11). We have not learned, however, of any other case in which there was a massive mediastinal lesion without communication with a contiguous bone.

#### SUMMARY

A case of multiple myeloma with extraosseous lesions is reported.

One of these lesions simulated a bronchogenic carcinoma or a lymphoma radiographically and for a time these diagnoses were considered.

The frequency of extraosseous lesions in multiple myeloma is emphasized.

ACKNOWLEDGMENT: The excellent editorial assistance of Mr. William S. Cornwell in preparation of this case report is acknowledged.

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## SUMMARIO IN INTERLINGUA

## Infiltration Extraossee in Myeloma Multiple

In le bizarre morbo, myeloma multiple, le possibilitate de lesiones in histos molle es frequentemente negligite. Es reportate un caso, necropticamente provate, que esseva remarcabile a causa de su extense affectiones myelomatose in omne partes del corpore. Del altere latere, illo exhibiva non plus que un sol lesion ossee,

un arrondate area osteolytic in le cranio. Un lesion pulmonar simulava un carcinoma bronchogene, o un lymphoma, e iste possibilitates diagnostic esseva considerate durante un certe tempore. Le caso esseva complicate additionalmente per le presentia de un carcinoma papillari del vesica.



# Vital Staining with Alizarin in Clinical Malignant Conditions of Bone<sup>1</sup>

S. SCHORR, M.D., I. AVIAD, M.D., and A. LAUFER, M.D.

**M**ADDER, OR *Rubia tinctorum*, is a plant which has been known for centuries. A marked staining of the growing ends of all bones in young animals was obtained with madder. The teeth were stained at their roots.

In 1736 Belchier (1) noted that bones of cooked pork had a reddish tinge, assuming, correctly, that madder was the factor that reddened the bones of the pigs. Duhamel (4), in 1739, introduced the coloring of growing bone with madder in ossification studies. Alizarin was recognized as the principal staining ingredient of the plant in 1826, by Robiquet and Colin (11). In 1869 alizarin was synthesized.

Gottlieb (6), in 1914, expressed the belief that alizarin has a specific chemical affinity for calcium. According to Cameron (1930) the tinctorial effect in the hard tissues is due to the property of alizarin to form a dye-lake with calcium, for which it is nearly a specific stain. Schour *et al.* (12) (1941) state that alizarin has a selective staining effect upon the calcifying or calcio-receptive zone of the collagenous matrix where calcium salts are being deposited.

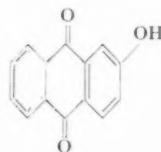
Vital staining with alizarin was applied in experimental studies of pathological calcifications, such as fractures and callus formation, by Brooks (2) in 1917, and to calcareous deposits in the aorta in 1932, by Ham (5). Cameron's (3) extensive investigations included staining of artificial deposits of calcium, fractures, calcium "casts" in the kidney, regenerating bone and calcified tissue, pathological calcification in hypervitaminosis, and calcification of the kidney following ligation of the renal vessels.

It was our purpose to study the behavior of alizarin as a staining material in malignant bone conditions *in vivo*, and to that

end injections of alizarin were given to patients with metastatic bone lesions. We considered the possibility that even in the osteolytic type of metastasis there may exist new bone formation, which possibly could be identified by this vital-staining method. Our assumption of new bone formation in malignant osteolytic bone metastases seemed to be substantiated by the staining of the metastatic areas with the dye. Even minute metastatic deposits measuring as little as 1 mm., not demonstrable by plain radiography, could be detected by alizarin vital staining. It was obvious, therefore, that it would be worthwhile looking for a chemical iodine-alizarin compound as a radiopaque substance and a radioactive iodine-alizarin compound for eventual diagnostic or therapeutic purposes. Chemical preparations are being investigated; an account of them will be given in a separate paper.

No clinical or experimental bone studies with alizarin in malignant conditions in man have so far been described in the literature.

**Chemistry:** The general formula of alizarin is



1,2-dihydroxyanthraquinone. It exists in madder as a glucoside, together with purpurin and purpurin 3-carboxylic acid. The sodium salt of alizarin, monosulfonic 1,2-dihydroxy-3-sodium sulfonic anthraquinone, is called Alizarin Red S. The sulfonic acid group renders this preparation much more soluble than pure

<sup>1</sup> From the X-Ray Department of the Municipal Hadassah Hospital, Tel-Aviv, and the Department of X-ray and Pathology of the Hadassah University Hospital, Jerusalem, Israel. Supported by a grant from the James Picker Foundation. Paper received for publication in September 1958.

alizarin, and for that reason Alizarin Red S was used in our studies.

#### CLINICAL MATERIAL

Alizarin Red S was injected in 15 patients with different types of malignant tumors metastasizing to bone, between January 1956 and September 1958. Three cases out of 6 which came to autopsy will be described and illustrated in this paper.

CASE I: K. K., a 58-year-old female with an inoperable right breast cancer, received deep x-ray irradiation accompanied by hormone therapy. Roentgen study of the skeleton showed radiolucent foci in the pelvic bones and in the left major trochanter. The patient received two drip-infusions, each of 2 gm. of Alizarin Red S in 500 c.c. of normal saline (20 drops per minute), with an interval of one week between the infusions. No toxic side-effects were seen except for a transient moderate nausea. The skin and mucous membranes, as well as the excreta, were red-stained for about twenty-four hours. The patient, who was in an extreme cachectic state, died ten days after the second injection. Autopsy showed an intraductal carcinoma of the right breast and multiple osteolytic foci in the skull, ribs, lumbar vertebrae, and pelvic bones. There were metastases also in the mediastinum, lungs, pleurae, pericardium, adrenals, and ovaries. The metastatic foci in the skull, ribs, and vertebrae were stained a purplish-red color. The stained lesions were well defined, with clear-cut borders. The "normal" bone between the lesions was not stained (Fig. 1).

*To summarize:* Alizarin Red S was injected into a 58-year-old female who had diffuse osteolytic bone metastases secondary to carcinoma of the breast. The metastatic osteolytic bone foci were well stained by the dye, with well limited sharp borders.

CASE II: P. N., a 62-year-old male, underwent a retropubic prostatectomy for an adenocarcinoma of the prostate in January 1953. Five months after the operation an x-ray study of the pelvic bones and lumbar vertebrae revealed multiple osteoplastic metastases. Orchiectomy was performed, followed by stilbestrol treatment. In January 1956, x-ray study of the pelvic bones, vertebrae, ribs, and femora showed an increase in size and number of the metastatic foci. A total of 5 gm. of Alizarin Red S in 2,500 c.c. of normal saline were injected on two separate occasions when the patient was hospitalized, on Feb. 9 and 11, 1956 (first admission), and on May 16 and 21 (second admission). Following the first injection a local irritation at the site of injection

was seen. After the second injection nausea and slight vomiting occurred. There was no toxic effect following the last two injections. Autopsy (Sept. 21, 1956), four months after the last injection, revealed multiple osteoplastic metastases in the pelvis, lumbar vertebrae, and ribs. The gross examination of longitudinal and transverse sections of the vertebrae disclosed diffuse irregular red-stained areas which corresponded to the osteoplastic foci seen in the roentgenogram. These stained areas were localized but not with sharply limited borders (Fig. 2). The reddish color was not uniform and faded gradually toward the surrounding bone. Ground sections revealed red-stained closely packed trabeculae which were irregularly distributed, mainly in the sclerotic lesions. Histologic study of these lesions showed metastatic carcinoma with osteoplastic changes which were mainly in the spongiosa. The cortex seemed to be well preserved and no dye was seen.

*To summarize:* Alizarin Red S was injected into a 62-year-old male who had diffuse osteoplastic bone metastases secondary to cancer of the prostate. The metastatic osteoplastic bone foci were well stained, with unsharp borders, the dye fading toward the "normal" surrounding bone.

CASE III: M. M., a 65-year-old female, gave a six-month history of neurologic signs and low back pain. Roentgenograms of the pelvic bones showed multiple osteolytic foci in the upper and the lower rami of the pubic bones. Alizarin Red S (5 gm. in 1,500 c.c. of normal saline) was given by drip infusion. Twelve days after the injection the patient died and an autopsy was performed. Reticulum-cell sarcoma of the lymph nodes was diagnosed (Dr. M. Loewenthal). On gross examination of the cut surface of the pelvic bones multiple major and minor well stained foci, grading from pink to dark red, were found throughout. In the iliac bone even minute foci of 1 to 2 mm. were well localized and clearly seen (Figs. 4 and 5). On comparison of the findings on gross examination with the roentgenograms, small foci which could not be visualized on the films were seen to be well stained by alizarin and clearly defined. Ground sections of bone specimens revealed a very active new bone formation at the site of the metastatic foci. The newly formed trabeculae, which were stained, were irregular in shape and size, forming a net-like structure (Fig. 6). These trabeculae varied in number in different areas of the same section. Their staining ranged from pale pink, with only few osteocytes, to an intensive purple color, with multiple osteocytes, possibly according to their different age and activity. The alizarin-stained ground sections were counterstained by methylene blue. With this technic it was possible to see that

Fig. 1. Case I: Osteolytic metastases from intraductal carcinoma of the breast. Sections obtained at autopsy from parietal bone and rib following intravenous vital staining with Alizarin Red S. Note the well stained metastatic foci with rather sharp borders and the unstained "normal" bone between the stained areas.

Fig. 2. Case II: Osteoplastic metastases from adenocarcinoma of the prostate. Specimen of lumbar vertebra obtained at autopsy following intravenous vital staining with alizarin. Note the stained osteosclerotic foci of various gradations, with unsharp borders.

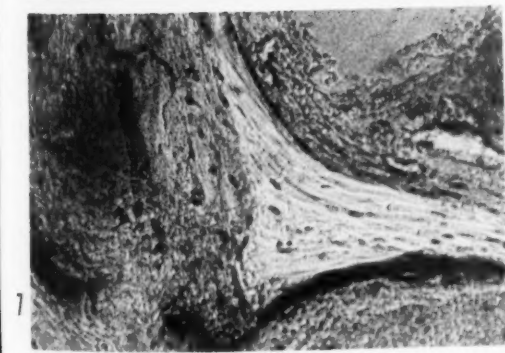
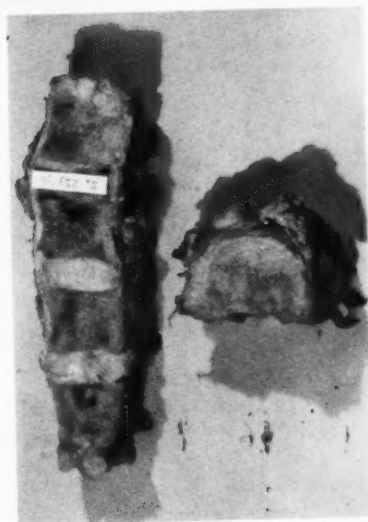
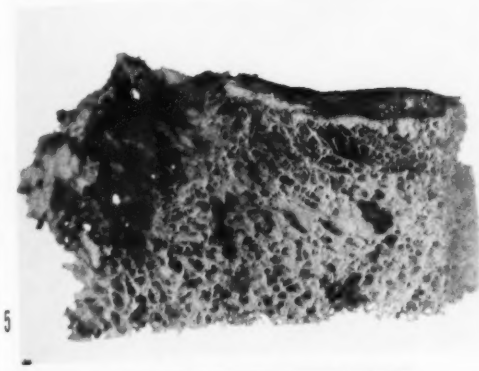
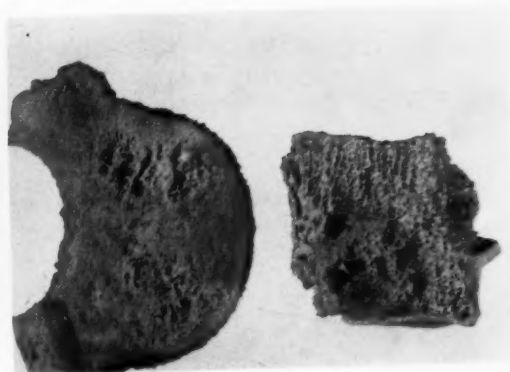
Fig. 3. Cases I and II: Macerated bone specimen from a longitudinal section of the second lumbar vertebra of Case I (osteolytic lesion). Note the intensively stained solitary lesion with its sharp borders in contrast to the surrounding unstained "normal" bone. Macerated bone specimen from a transverse section of the third lumbar vertebra of Case II (osteoplastic lesion). Note the multiple stained osteosclerotic areas with unsharp borders.

Fig. 4. Case III: Reticulum-cell sarcoma. Section of right iliac bone obtained at autopsy. Even minute foci, measuring less than 1.0 mm., are stained intensively.

Fig. 5. Case III: Same specimen as in Fig. 4 after maceration.

Fig. 6. Case III: Ground section from the iliac bone. Note network of newly formed trabeculae stained intensively, in and around an osteolytic focus, in contrast to the old, unstained trabeculae.

Fig. 7. Case III: Ground section from iliac bone counterstained by methylene blue. Note the apposition of well stained new bone and unstained old trabeculae.





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the collagen fibers were well stained by methylene blue and the new bone trabeculae were stained red or pink by alizarin. In addition, the osteocytes were stained blue in contrast to the red-stained osteoid tissue (Fig. 7). An impression might be gained that we deal with a gradual passage from collagen through osteoid formation to osteosclerosis. In some places there may be seen newly formed trabeculae occupying a space filled with malignant cells. The fact that a graded coloration was seen is probably due to a rapid bone growth that takes place in the tumor area. The old normal shaped trabeculae were not stained. In other places there were nonstained old trabeculae with apposition of intensively stained new bone (Fig. 7). The cartilage and the capillaries were not stained.

*To summarize:* Alizarin Red S was injected into a 65-year-old female having reticulum-cell sarcoma with diffuse osteolytic foci in the pelvic bones. Even minute foci which were not detected on the roentgenograms were well stained by the dye. The newly formed irregular, coarse, thickened trabeculae were well stained.

In the three cases reported above, Alizarin Red S was given intravenously. The autopsy showed marked staining of the metastatic lesions, both osteolytic and osteoplastic. It may be assumed from these observations that no qualitative differences exist between osteolytic and osteoplastic bone conditions, in so far as the selectivity of alizarin is concerned. Both predominantly destructive and predominantly productive malignant metastases have a definite affinity for vital staining by Alizarin Red S. It was shown that considerable bone formation exists even in the osteolytic foci, though in small amounts not detectable by x-ray examination.

*Toxicological Observations:* Alizarin Red S administered intravenously in a dose of 60-70 mg. per kilogram of body weight produces no significant toxic effects. There occurs, however, a severe nausea accompanied occasionally by vomiting, red coloration of the skin, mucous membranes, and excreta, which may last for twenty-four to forty-eight hours. Since alizarin is excreted mainly through the kidneys, it is contraindicated in patients having chronic or acute renal disease.

#### DISCUSSION

Very little is yet known concerning the selective staining of bone with alizarin. The fact that decalcification results in complete loss of the staining phenomenon shows that the effect of alizarin is due to its union with the calcium salts of the bone. Cameron, in his basic studies on the subject, concludes that selective staining of bone with alizarin administered experimentally during life is common in all vertebrates. His observations show that the concentration of the alizarin in pathological deposits of calcium salts is in close agreement with that found in physiological deposits in bone. Alizarin reaches the deposit by way of the tissue fluids and unites with any calcium that is available at the time of the staining. There is no evidence that cellular activity plays any part in the deposition of alizarin in an area of calcification. Neither is there any direct dependence on vascularity. Newly formed bone stains much more intensively than fully formed mature bone. It appears that recently deposited inorganic salts are easily stained with alizarin by way of the blood, while old deposits stain with difficulty. The nature of the arrangement of the calcium complexes may be different in young and old deposits. According to Macklin (7), the areas more deeply stained are composed of freshly deposited calcium salts. According to von Möllendorf (10) the coloration is due to the formation of calcium alizarinate in bone.

Cancer metastases in bone are frequently thought to be divisible into two presumably distinct roentgenographic types: the "osteolytic" type characterized by relative radiolucency and the "osteoplastic" type characterized by relative radiopacity. According to Milch (8), there is no essential histologic difference in so far as the host bone is concerned in respect to so-called "osteolytic" and so-called "osteoplastic" metastases; the histological appearance in each instance is distinct only in a quantitative sense. Qualitatively, the histologic appearance of predominantly destructive and predominantly productive

cancer metastases is identical. Differences in bone response to the invasion of the various types of neoplasm are merely differences in degree and not in kind.

Biological and histologic data concerning "osteolytic" or "osteoplastic" phenomena in bone are infrequently reported in the literature (8). The vital staining by alizarin could eventually serve as a biologic test, indicating the intensity of new bone formation in both types of malignant condition. It appears from the cases described that there exists a marked new bone formation even in the so-called "osteolytic" type.

The cases described above had secondary metastatic bone lesions. Alizarin was also injected into a patient with multiple myeloma, but no response of newly formed bone tissue was detected. As might have been anticipated, no alizarin staining was seen in and around the osteolytic foci. This lack of staining is an additional indirect proof of the strong affinity between new bone formation and vital staining with alizarin.

It has been established that bone neoplasms involve an abnormally high metabolic turnover of metal ions, in particular calcium ions (13). The malignant cells follow in their metabolic behavior the pattern of rapidly growing cells. It seems reasonable that any method which demonstrates the increased metabolic turnover of the neoplastic tissues may be applied for localization of bone tumors.

No basic work has so far been done on alizarin metabolism in laboratory animals. We do not know the exact percentage which is fixed in the normal young animal and the quantity which is excreted in the urine, feces, etc. The amount which is fixed in the skeleton, and especially in the bone lesions, has therefore still to be studied. This basic investigation is important in order to determine the iodine quantity and its concentration in these lesions.

The high uptake of alizarin in areas where new bone is being laid down may indicate that radioactive iodoalizarin will provide a valuable tool in the study of ac-

tive new bone formation whether in "normal" anatomic-physiologic bone formation or in inflammatory, traumatic, and neoplastic bone conditions. Study with radioactive alizarinate compounds could provide a vital biologic method for determination and correlation between chemical blood studies and the rate of laying down of new bone tissue, in different physiologic and pathologic conditions.

De-alizarination follows decalcification, *i.e.*, the localized pink color of the malignant bone lesions fades away. Therefore, the fresh bone preparations are cut to slices about 1 mm. in thickness by means of a saw and ground down manually to a thickness of about 10–20  $\mu$ . The study of a ground section preparation is rendered difficult by the fact that in these bone disks, superimposition of trabeculae is present and may result in certain artefacts.

#### SUMMARY

Alizarin Red S, a well known vital staining substance for growing bone, was injected intravenously into adult patients with metastatic malignant bone lesions of the osteolytic and osteoplastic type. This was the first use of an intravital staining method in patients.

Postmortem examination showed that the metastatic bone foci were stained intensively.

It was shown that there exists an active new bone formation in and around malignant bone lesions even when these are predominantly osteolytic. The newly formed bone trabeculae seen by this vital staining method are thickened and irregular, and invade the destroyed areas. The old trabeculae were not stained, whereas the newly formed bone in apposition to the old tissue was stained intensively. The difference between osteolytic and osteoplastic foci in respect to new bone formation as demonstrated by alizarin staining is only quantitative.

ACKNOWLEDGMENT: We are indebted to A. Hochman, M.D., Head of the Radium Therapy Department of the Hadassah University Hospital, Jerusalem, to M. Loewenthal, M.D., Head of the Department of Pathology, Hadassah Municipal Hospital,

Tel-Aviv, to H. Ungar, M.D., Prof. of Pathology, for reviewing the sections and to Mr. H. Reuveni for the photographic work.

The authors are most grateful to Leo G. Rigler, M.D., for help in reviewing this paper.

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#### SUMMARY IN INTERLINGUA

##### Tincturation Vital con Alizarina in Conditiones Maligne Clinic de Osso

Alizarina rubie S, un ben cognoscite substantia de tincturation vital pro osso crescente, esseva injicite per via intravenose in patientes adulte con metastatic lesiones maligne de osso del typos osteolytic e osteoplastic. Isto esseva le prime uso de un methodo de tincturation intravital in patientes human.

Examines necroptic monstrava que le focos de metastase ossee esseva tincturate intensemente.

Esseva provate que il existe un active formation de osso nove in e circum le maligne lesiones ossee mesmo quando istos

es predominantemente osteolytic. Le novemente formate trabeculas de osso que esseva demonstrate per iste methodo de tincturation vital se monstrava spissificate e irregular e invadeva le areas de destruction. Le ancian trabeculas non habeva acceptate le tincturation, durante que le novemente formate osso in apposition al ancian histos esseva tincturate intensemente. Le differentia inter focos osteolytic e focos osteoplastic con respecto al neoformation demonstrate per tincturation a alizarina es solmente quantitative.



## Dosage Tables for Linear Radium Sources Filtered by 0.5 and 1.0 mm. of Platinum<sup>1</sup>

M. A. GREENFIELD, Ph.D., M. FICHMAN, B.S., and A. NORMAN, Ph.D.

THE DOSAGE tables for linear radium sources filtered by 0.5 mm. platinum computed by Quimby (1) continue to be extremely useful in the planning of radium therapy. No corresponding table exists, however, for linear sources filtered by 1.0 mm. of platinum, which are also commonly used in radium therapy. We have computed such a table, therefore, using Sievert's integrals (2). An extensive check of the table by application of the principles of symmetry and similitude (see below) shows that the computed dose rates are internally consistent to about 1 per cent. A similar check of Quimby's table (1) reveals inconsistencies of the order of 10 per cent. To remove these inconsistencies we have also computed a dosage table for linear radium sources filtered by 0.5 mm. platinum.

The tables are presented in the same form as that used by Quimby. Readers are referred to her paper (1) or to the standard text of Glasser *et al.* (3) for instructions as to their use.

### METHOD

The tables were computed by linear interpolation from Sievert's integrals. Absorption coefficients used were  $0.15 \text{ cm.}^{-1}$  for radium sulfate,  $2.00 \text{ cm.}^{-1}$  for 0.5 mm. platinum and  $1.94 \text{ cm.}^{-1}$  for 1.0 mm. platinum (2). The radium was assumed to be uniformly distributed on a thin line at the center of the needle. The thickness of the radium salt was taken as the difference between the measured needle thickness and the thickness of the platinum filter. For 1.0 mm. and 0.5 mm. Pt, the radium sulfate thicknesses were, respectively, 1.5 and 0.65 mm. A value of  $9.33 \text{ r/mg.-hr.}$  was taken as the dose rate 1.0 cm. from an unfiltered source of radium. This value is consistent with the figure of  $8.4 \text{ r/mg.-hr.}$

from a point source of radium filtered by 0.5 mm. of platinum and is in satisfactory agreement with both calculated and experimental values (4). The scattering and absorption of the gamma rays in tissue was ignored.

A thorough investigation of the tables applying principles of symmetry and similitude (see below) indicates an internal consistency of 1.0 per cent or better throughout. At least half the entries were checked in this way. In addition, all entries were checked graphically. Assuming the validity of the basic assumptions, the accuracy is about 1 per cent for those regions in which the dose rate is in excess of  $0.2 \text{ r/mg.-hr.}$  In the regions where the dose rates are smaller, Sievert's integrals lead to small differences in two large numbers, so that the inaccuracies are somewhat larger. Fortunately, in the low dose rate regions far from the needles, high degrees of accuracy are not necessary.

The symmetry principle is readily demonstrated by the following example: the dose rate from the center of a 2.0-cm. needle should be exactly the same as the intensity from the end of a 1.0-cm. needle with the same total radium content. At a distance of 0.75 cm. from the center of a 2.0-cm. needle the dose rate from Quimby's table is  $11.11 \text{ r/mg.-hr.}$  whereas at 0.75 cm. from the end of a 1.0-cm. needle the dose rate is given as  $9.50 \text{ r/mg.-hr.}$  In our table for 0.5 mm. platinum filter the dose rate in each case is  $10.2 \text{ r/mg.-hr.}$

The principle of similitude can be illustrated by the following example: 1 cm. from the center of a 1-cm. needle we expect the dose rate to be exactly one-fourth that found 0.5 cm. from a 0.5-cm. needle. (It is clear that the triangle formed by the 1.0-cm. needle and the point 1 cm. distant from its center is similar to the triangle formed by

<sup>1</sup> From the Department of Radiology, University of California, Los Angeles, Calif. Accepted for publication in October 1958.



the 0.5-cm. needle and the point 0.5-cm. away. The physical distances involved differ, however, by a factor of two, and the dose rates, therefore, differ by a factor of four). In Meredith's table (5) for 1.0 mm. of platinum, the dose rates for the two cases are given as 33 mg.-hr./1,000 r or 30.3 r/mg.-hr., and 143 mg.-hr./1,000 r or 6.99 r/mg.-hr. In our table the two dose rates are 27.9 r/mg.-hr. and 6.99 r/mg.-hr. There is a factor of 4.3 between the dose rates in Meredith's table and a factor of 4.0, as required by the geometry of the situation, between the corresponding dose rates in our table.

Clearly the tables are readily extensible by application of the principles of symmetry and similitude. The dose rates that

we have computed are presented in the tables on pages 420-423.

Note: The authors thank Mr. Carl Chamberlain for his help in checking the tables.

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#### SUMMARIO IN INTERLINGUA

##### Tabulas de Dosage pro Fontes Linear de Radium Filtrate per 0,5 e 1,0 mm de Platino

Tabulas de dosage pro fontes linear de radium filtrate per 0,5 mm de platino esseva computate per Quimby e se ha provate multo utile in le planar de therapia a radium. Fontes linear filtrate per 1,0 mm de platino es etiam de uso commun in le therapia a radium. Per consequente le presente autores ha computate un tabula pro tal fontes, utilisante le integrales de Sievert. Extense probas del tabula, ef-

fectuate per le application del principios de symmetria e similitude, ha monstrate que le computate dosages es internemente exacte intra circa 1 pro cento.

Un tabula de dosage pro fontes linear filtrate per 0,5 mm de platino esseva etiam construite e es considerate como plus accurate que le tabula de Quimby. Iste tabulas es presentate in le mesme forma como illo usate per Quimby.

(For tables see pp. 420-423)

TABLE I: ROENTGENS PER MG.-HR. DELIVERED AT VARIOUS DISTANCES BY LINEAR RADIUM SOURCES FILTERED BY 0.5 MM. Pt

Distance from Tube (cm.)	Distance Along Tube Axis (cm. from Center)										
	0	0.5	1.0	1.5	2.0	2.5	3.0	3.5	4.0	4.5	5.0
Active length 0.5 cm.											
0.5	31.0	16.8	6.10	2.84	1.46	0.86	0.56	0.34	0.26	0.19	0.15
0.75	14.4	10.2	5.15	2.64	1.55	0.97	0.65	0.45	0.32	0.25	0.20
1.0	8.26	6.63	4.08	2.38	1.49	0.98	0.69	0.49	0.35	0.28	0.21
1.5	3.68	3.31	2.55	1.80	1.24	0.90	0.66	0.47	0.40	0.30	0.24
2.0	2.09	1.97	1.66	1.32	1.00	0.78	0.60	0.47	0.36	0.30	0.24
2.5	1.34	1.29	1.16	0.97	0.81	0.64	0.53	0.41	0.35	0.28	0.24
3.0	0.93	0.90	0.83	0.74	0.65	0.54	0.44	0.38	0.31	0.27	0.22
4.0	0.53	0.52	0.49	0.46	0.41	0.36	0.33	0.29	0.25	0.22	0.19
5.0	0.34	0.33	0.33	0.31	0.29	0.27	0.24	0.22	0.20	0.17	0.16
Active length 1.0 cm.											
0.5	26.0	18.2	6.96	3.00	1.55	0.88	0.58	0.37	0.22	0.17	0.11
0.75	13.1	10.2	5.48	2.82	1.60	1.01	0.65	0.45	0.35	0.25	0.19
1.0	7.80	6.54	4.20	2.49	1.52	1.01	0.71	0.50	0.36	0.27	0.21
1.5	3.61	3.27	2.57	1.83	1.29	0.91	0.66	0.50	0.39	0.30	0.24
2.0	2.07	1.95	1.66	1.33	1.03	0.77	0.60	0.47	0.37	0.29	0.25
2.5	1.33	1.28	1.15	0.98	0.80	0.65	0.52	0.43	0.35	0.28	0.24
3.0	0.92	0.90	0.83	0.74	0.64	0.54	0.45	0.37	0.32	0.27	0.23
4.0	0.52	0.52	0.49	0.46	0.41	0.37	0.33	0.29	0.25	0.22	0.19
5.0	0.34	0.33	0.32	0.31	0.29	0.27	0.24	0.22	0.20	0.18	0.16
Active length 1.5 cm.											
0.5	21.7	18.0	8.58	3.46	1.72	0.96	0.60	0.39	0.26	0.16	0.11
0.75	11.6	9.89	6.00	3.11	1.72	1.05	0.70	0.47	0.34	0.26	0.18
1.0	7.12	6.33	4.37	2.64	1.64	1.05	0.72	0.51	0.37	0.28	0.22
1.5	3.48	3.22	2.56	1.86	1.31	0.94	0.68	0.51	0.38	0.31	0.24
2.0	2.01	1.90	1.66	1.33	1.03	0.79	0.61	0.48	0.38	0.30	0.25
2.5	1.31	1.26	1.14	0.98	0.80	0.66	0.53	0.43	0.35	0.29	0.24
3.0	0.91	0.89	0.82	0.74	0.64	0.54	0.45	0.38	0.31	0.27	0.23
4.0	0.52	0.51	0.49	0.46	0.41	0.37	0.33	0.30	0.26	0.22	0.20
5.0	0.33	0.33	0.32	0.31	0.29	0.27	0.24	0.22	0.20	0.18	0.16
Active length 2.0 cm.											
0.5	18.2	16.7	10.6	4.27	1.95	1.06	0.63	0.40	0.27	0.17	0.12
0.75	10.2	9.27	6.51	3.55	1.92	1.13	0.73	0.50	0.35	0.27	0.19
1.0	6.54	6.04	4.55	2.85	1.74	1.12	0.76	0.53	0.39	0.29	0.22
1.5	3.27	3.09	2.55	1.92	1.37	0.98	0.71	0.53	0.40	0.31	0.25
2.0	1.95	1.85	1.64	1.33	1.05	0.81	0.62	0.48	0.38	0.31	0.25
2.5	1.28	1.24	1.13	0.97	0.81	0.66	0.53	0.44	0.35	0.29	0.25
3.0	0.90	0.88	0.82	0.74	0.64	0.55	0.46	0.38	0.32	0.27	0.23
4.0	0.52	0.51	0.49	0.45	0.41	0.38	0.33	0.29	0.26	0.21	0.19
5.0	0.33	0.33	0.32	0.31	0.29	0.27	0.24	0.22	0.20	0.18	0.16

TABLE I: ROENTGENS PER MG.-HR. DELIVERED AT VARIOUS DISTANCES BY LINEAR RADIUM SOURCES FILTERED BY 0.5 MM. Pt—cont.

Distance from Tube (cm.)	Distance Along Tube Axis (cm. from Center)										
	0	0.5	1.0	1.5	2.0	2.5	3.0	3.5	4.0	4.5	5.0
Active length 2.5 cm.											
0.5	15.4	14.7	11.6	5.63	2.36	1.22	0.69	0.44	0.28	0.19	0.13
0.75	9.00	8.50	6.76	4.10	2.19	1.25	0.79	0.53	0.37	0.26	0.20
1.0	5.95	5.63	4.59	3.13	1.92	1.21	0.80	0.56	0.40	0.30	0.23
1.5	3.10	2.95	2.53	1.97	1.43	1.01	0.74	0.54	0.42	0.32	0.26
2.0	1.87	1.81	1.61	1.34	1.07	0.84	0.64	0.50	0.39	0.31	0.26
2.5	1.25	1.21	1.11	0.96	0.82	0.67	0.54	0.43	0.36	0.28	0.24
3.0	0.88	0.86	0.81	0.73	0.64	0.55	0.46	0.39	0.33	0.27	0.23
4.0	0.51	0.50	0.48	0.45	0.41	0.38	0.33	0.30	0.26	0.22	0.20
5.0	0.33	0.33	0.32	0.30	0.29	0.27	0.24	0.22	0.20	0.18	0.16
Active length 3.0 cm.											
0.5	13.5	13.1	11.6	7.25	3.04	1.42	0.79	0.47	0.31	0.21	0.14
0.75	8.00	7.73	6.70	4.66	2.58	1.43	0.87	0.57	0.39	0.28	0.22
1.0	5.43	5.21	4.53	3.37	2.15	1.33	0.87	0.60	0.43	0.31	0.24
1.5	2.90	2.81	2.48	2.01	1.51	1.07	0.78	0.57	0.43	0.34	0.26
2.0	1.78	1.74	1.58	1.35	1.09	0.86	0.66	0.51	0.41	0.32	0.26
2.5	1.21	1.18	1.09	0.97	0.82	0.68	0.56	0.45	0.37	0.30	0.25
3.0	0.86	0.84	0.80	0.73	0.64	0.55	0.47	0.40	0.33	0.28	0.24
4.0	0.50	0.50	0.48	0.45	0.41	0.37	0.33	0.29	0.26	0.23	0.20
5.0	0.33	0.32	0.32	0.30	0.29	0.27	0.24	0.22	0.20	0.18	0.16
Active length 4.0 cm.											
0.5	10.6	10.5	9.99	8.79	5.56	2.33	1.10	0.62	0.37	0.25	0.17
0.75	6.50	6.39	6.04	5.20	3.61	2.02	1.13	0.70	0.46	0.32	0.23
1.0	4.55	4.45	4.16	3.58	2.63	1.69	1.06	0.70	0.49	0.36	0.27
1.5	2.55	2.51	2.32	2.03	1.63	1.22	0.88	0.64	0.48	0.36	0.28
2.0	1.64	1.59	1.50	1.33	1.13	0.91	0.71	0.56	0.43	0.35	0.28
2.5	1.13	1.10	1.04	0.95	0.83	0.70	0.58	0.48	0.39	0.32	0.26
3.0	0.82	0.81	0.77	0.71	0.64	0.56	0.48	0.41	0.34	0.29	0.24
4.0	0.49	0.48	0.46	0.44	0.41	0.37	0.33	0.30	0.26	0.23	0.20
5.0	0.32	0.32	0.31	0.30	0.28	0.26	0.24	0.22	0.20	0.18	0.17
Active length 5.0 cm.											
0.5	8.62	8.59	8.45	8.09	7.13	4.52	1.91	0.90	0.51	0.31	0.21
0.75	5.45	5.40	5.26	4.94	4.24	2.95	1.65	0.93	0.58	0.39	0.27
1.0	3.86	3.84	3.71	3.41	2.93	2.16	1.40	0.89	0.60	0.41	0.31
1.5	2.26	2.23	2.14	1.97	1.70	1.37	1.02	0.75	0.55	0.41	0.31
2.0	1.48	1.47	1.40	1.29	1.14	0.96	0.78	0.61	0.49	0.38	0.30
2.5	1.04	1.03	0.99	0.90	0.83	0.72	0.61	0.51	0.42	0.34	0.28
3.0	0.77	0.76	0.73	0.69	0.63	0.56	0.49	0.42	0.36	0.30	0.26
4.0	0.47	0.46	0.45	0.43	0.40	0.37	0.34	0.30	0.27	0.24	0.21
5.0	0.31	0.31	0.30	0.29	0.28	0.26	0.24	0.22	0.20	0.19	0.17

TABLE II: ROENTGENS PER MG.-HR. DELIVERED AT VARIOUS DISTANCES BY LINEAR RADIUM SOURCES FILTERED BY 1.0 MM. Pt

Distance from Tube (cm.)	Distance Along Tube Axis (cm. from Center)										
	0	0.5	1.0	1.5	2.0	2.5	3.0	3.5	4.0	4.5	5.0
Active length 0.5 cm.											
0.5	27.9	14.7	4.97	1.98	1.01	0.52	0.34	0.15	0.15	0.08	0.03
0.75	12.9	9.07	4.41	2.12	1.17	0.70	0.40	0.30	0.20	0.15	0.08
1.0	7.41	5.91	3.53	2.02	1.18	0.75	0.50	0.35	0.22	0.21	0.11
1.5	3.31	3.02	2.24	1.57	1.06	0.73	0.54	0.39	0.27	0.22	0.12
2.0	1.88	1.79	1.48	1.15	0.89	0.65	0.51	0.35	0.33	0.22	0.18
2.5	1.21	1.16	1.03	0.88	0.69	0.57	0.45	0.35	0.28	0.23	0.19
3.0	0.84	0.81	0.75	0.66	0.56	0.46	0.39	0.32	0.27	0.22	0.18
4.0	0.47	0.46	0.45	0.41	0.37	0.33	0.29	0.25	0.22	0.18	0.16
5.0	0.30	0.30	0.29	0.27	0.26	0.23	0.21	0.19	0.18	0.15	0.14
Active length 1.0 cm.											
0.5	23.2	15.8	5.71	2.24	1.04	0.56	0.32	0.19	0.13	0.09	0.06
0.75	11.8	9.05	4.68	2.29	1.22	0.72	0.45	0.29	0.20	0.14	0.09
1.0	6.99	5.81	3.68	2.11	1.24	0.78	0.50	0.35	0.25	0.18	0.13
1.5	3.23	2.94	2.27	1.58	1.10	0.76	0.53	0.39	0.29	0.22	0.17
2.0	1.85	1.75	1.49	1.17	0.89	0.67	0.51	0.38	0.30	0.23	0.19
2.5	1.20	1.15	1.02	0.87	0.72	0.57	0.45	0.36	0.28	0.23	0.19
3.0	0.83	0.81	0.75	0.66	0.56	0.47	0.39	0.32	0.27	0.23	0.18
4.0	0.47	0.46	0.44	0.41	0.37	0.33	0.29	0.25	0.22	0.19	0.16
5.0	0.30	0.30	0.29	0.27	0.26	0.24	0.22	0.20	0.17	0.16	0.14
Active length 1.5 cm.											
0.5	19.1	15.8	7.75	2.65	1.17	0.62	0.34	0.21	0.12	0.09	0.05
0.75	10.3	8.77	5.19	2.56	1.32	0.75	0.46	0.30	0.22	0.14	0.10
1.0	6.41	5.62	3.79	2.25	1.32	0.81	0.53	0.35	0.26	0.18	0.14
1.5	3.12	2.86	2.26	1.64	1.10	0.79	0.55	0.40	0.30	0.22	0.17
2.0	1.81	1.71	1.47	1.16	0.89	0.68	0.51	0.40	0.30	0.24	0.18
2.5	1.18	1.13	1.01	0.86	0.71	0.57	0.46	0.36	0.29	0.24	0.19
3.0	0.82	0.80	0.74	0.66	0.56	0.47	0.39	0.33	0.27	0.23	0.19
4.0	0.47	0.46	0.44	0.41	0.37	0.33	0.29	0.26	0.22	0.19	0.17
5.0	0.30	0.30	0.29	0.28	0.26	0.24	0.21	0.20	0.18	0.16	0.14
Active length 2.0 cm.											
0.5	15.8	14.5	9.05	3.50	1.40	0.68	0.37	0.22	0.14	0.09	0.06
0.75	9.07	8.24	5.66	2.96	1.50	0.84	0.50	0.32	0.21	0.14	0.11
1.0	5.81	5.30	3.94	2.41	1.42	0.87	0.56	0.37	0.26	0.19	0.14
1.5	2.94	2.75	2.26	1.67	1.17	0.82	0.57	0.41	0.31	0.23	0.18
2.0	1.75	1.67	1.45	1.17	0.92	0.70	0.53	0.40	0.31	0.24	0.20
2.5	1.15	1.11	1.01	0.86	0.71	0.59	0.46	0.37	0.30	0.24	0.19
3.0	0.81	0.79	0.73	0.65	0.57	0.48	0.39	0.33	0.28	0.23	0.19
4.0	0.46	0.46	0.44	0.41	0.37	0.33	0.29	0.26	0.22	0.19	0.17
5.0	0.30	0.30	0.29	0.27	0.26	0.23	0.22	0.20	0.18	0.16	0.14

# DOSAGE TABLES FOR LINEAR RADIUM SOURCES

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TABLE II: ROENTGENS PER MG.-HR. DELIVERED AT VARIOUS DISTANCES BY LINEAR RADIUM SOURCES FILTERED BY 1.0 MM. PT—cont.

TABLE II: KOENTGENS PER MINUTE BY 1.0 MM. PT.—cont.											
Distance from Tube (cm.)	Distance Along Tube Axis (cm. from Center)										
	0	0.5	1.0	1.5	2.0	2.5	3.0	3.5	4.0	4.5	5.0
Active length 2.5 cm.											
0.5	13.3	12.8	10.1	4.65	1.76	0.80	0.51	0.25	0.15	0.09	0.06
0.75	7.95	7.50	5.94	3.49	1.75	0.93	0.55	0.35	0.22	0.16	0.11
1.0	5.26	4.94	3.99	2.67	1.59	0.96	0.60	0.40	0.28	0.20	0.15
1.5	2.77	2.62	2.23	1.71	1.22	0.86	0.60	0.43	0.32	0.23	0.18
2.0	1.68	1.61	1.43	1.19	0.93	0.72	0.55	0.41	0.32	0.24	0.20
2.5	1.12	1.08	0.99	0.86	0.72	0.59	0.47	0.38	0.30	0.24	0.20
3.0	0.79	0.78	0.73	0.65	0.56	0.48	0.40	0.34	0.28	0.23	0.19
4.0	0.46	0.45	0.43	0.40	0.37	0.33	0.29	0.26	0.22	0.19	0.17
5.0	0.30	0.29	0.29	0.27	0.25	0.24	0.22	0.20	0.18	0.16	0.14
Active length 3.0 cm.											
0.5	11.5	11.1	10.0	6.22	2.38	1.00	0.50	0.28	0.17	0.10	0.07
0.75	7.05	6.77	5.88	4.01	2.12	1.10	0.62	0.38	0.24	0.17	0.12
1.0	4.74	4.56	3.94	2.88	1.94	1.15	0.66	0.43	0.29	0.21	0.16
1.5	2.59	2.49	2.19	1.75	1.29	0.91	0.65	0.46	0.33	0.25	0.19
2.0	1.61	1.55	1.40	1.18	0.95	0.74	0.56	0.43	0.33	0.26	0.20
2.5	1.08	1.06	0.97	0.86	0.72	0.59	0.49	0.39	0.31	0.25	0.20
3.0	0.78	0.76	0.71	0.64	0.56	0.48	0.40	0.34	0.28	0.23	0.20
4.0	0.45	0.45	0.43	0.40	0.37	0.33	0.29	0.26	0.22	0.20	0.17
5.0	0.30	0.29	0.28	0.27	0.25	0.24	0.22	0.20	0.18	0.16	0.14
Active length 4.0 cm.											
0.5	9.05	8.97	8.64	7.60	4.69	1.82	0.77	0.39	0.21	0.13	0.08
0.75	5.70	5.58	5.26	4.52	3.09	1.64	0.86	0.49	0.30	0.20	0.14
1.0	3.94	3.86	3.61	3.09	2.25	1.40	0.88	0.53	0.35	0.24	0.17
1.5	2.26	2.21	2.05	1.78	1.41	1.04	0.74	0.53	0.38	0.27	0.21
2.0	1.45	1.42	1.32	1.18	0.98	0.78	0.60	0.47	0.35	0.28	0.22
2.5	1.01	0.99	0.93	0.84	0.73	0.61	0.50	0.41	0.33	0.26	0.21
3.0	0.73	0.72	0.69	0.63	0.56	0.49	0.42	0.35	0.29	0.24	0.20
4.0	0.44	0.43	0.42	0.39	0.36	0.33	0.29	0.26	0.23	0.20	0.17
5.0	0.29	0.29	0.28	0.27	0.25	0.23	0.22	0.20	0.18	0.16	0.15
Active length 5.0 cm.											
0.5	7.39	7.35	7.24	6.83	6.10	3.77	1.46	0.62	0.31	0.18	0.10
0.75	4.72	4.69	4.56	4.04	3.66	2.50	1.33	0.70	0.40	0.25	0.17
1.0	3.33	3.30	3.19	2.96	2.52	1.83	1.16	0.70	0.44	0.29	0.20
1.5	1.98	1.95	1.88	1.72	1.48	1.17	0.87	0.61	0.44	0.32	0.23
2.0	1.31	1.29	1.24	1.13	1.00	0.83	0.66	0.51	0.40	0.31	0.24
2.5	0.93	0.92	0.88	0.81	0.73	0.63	0.53	0.43	0.36	0.28	0.23
3.0	0.69	0.68	0.65	0.61	0.56	0.50	0.43	0.36	0.30	0.26	0.22
4.0	0.42	0.42	0.40	0.38	0.36	0.33	0.30	0.26	0.23	0.21	0.18
5.0	0.28	0.28	0.27	0.26	0.25	0.23	0.22	0.20	0.18	0.16	0.15



# Total-Body X-Irradiation and Splenectomy in Guinea-Pigs<sup>1</sup>

PIETRO de FRANCISCIS and EMILIO SCANZIANI

THE EXISTENCE OF a specific factor produced by spleen which enables the organism to adjust to different and dangerous situations has been admitted, although only as an hypothesis, since the early experiments of Barcroft (1-5) and Viale (6). Recently the experimental work of Rein (7-11), of Ungar (12) and of de Franciscis (13-17) has supported this hypothesis. Good demonstration of this particular action of the spleen was given by Cole (18-21), by Jacobson (22-25), and by Ungar (26), studying the protective action of spleen homogenate and of shielding of the spleen against radiation injuries. Raventos (27), on the other hand, although finding in a study on x-ray injuries that the post-irradiation mortality was slightly higher in splenectomized mice than in their unoperated or sham-operated controls, concluded that the difference was not great enough to warrant the supposition that any specific factor in the spleen promotes recovery after whole-body irradiation.

In planning an investigation of the relationship between radiation qualities and biological effect, it seemed to us important to study the effect of splenectomy on survival following exposure to different doses of x-rays.

## METHODS

The experiments were carried out, at various times in the past three years, on a total of 296 guinea-pigs, considered by Kohn (28) the most sensitive, among the experimental animals, to radiation injury. One hundred and thirty-three animals were splenectomized before being exposed to whole-body irradiation, the other 163 were irradiated intact.

The x-rays were generated by a 180 to 200-kv (Duoval-Siemens) machine, the presence of condensators and of a Liebe-

now-Greinacher circuit guaranteeing constancy in tension level. The half-value layer was determined on a field of 49 sq. cm. The thimble ionization chamber of a Siemens universal dosimeter was located 10 cm. distant from the tube. With 0.5 mm. Cu plus 3.0 mm. Al filtration, the half-value layer was 0.8 mm. Cu; when no filter was used, 0.3 mm. Cu.

The guinea-pigs were placed radially on a wooden tray 25 in. in diameter and 1/4 in. thick, lying on their backs, with their legs stretched out and tied. Care was taken to deliver a uniform dose of radiation to the splenic area. The total dosage was 650 r, 1,300 r, and 1,950 r, with and without filtration, at a rate of 4.4 r, 8.8 r, and 13 r per minute. Under these conditions, the amount of radiation absorbed by a paraffin layer 1.0 cm. thick was recorded for:

- 650 r, added filter, 4.4 to 4 r/min., focal distance 76 cm.
- 1,300 r, added filter, 8.8 to 8 r/min., focal distance 55 cm.
- 1,950 r, added filter, 13.2 to 11.8 r/min., focal distance 45 cm.
- 650 r, without filter, 4.4 to 3.8 r/min., focal distance 113 cm.
- 1,300 r, without filter, 8.8 to 7.8 r/min., focal distance 80 cm.
- 1,950 r, without filter, 13.2 to 11.6 r/min., focal distance 66 cm.

In view of the observations made, the superficial location of the spleen, and the thickness of the skin of the guinea-pig, it was not considered necessary to make any allowance for the radiation absorbed from the skin.

No anesthetic was used during irradiation. Splenectomy, however, was done under Nembutal anesthesia (5.0 mg., per 100 gm. of body weight injected intraper-

<sup>1</sup> From the Department of Human Physiology, University of Naples, and the Radiological Division, Principi di Piemonte Hospital, Naples, Italy Accepted for publication in October 1958.

TABLE I: EFFECT OF IRRADIATION IN NORMAL ANIMALS

X-Ray Dosage (r)	Filtering	Number of Animals	Mortality During Post-Irradiation Days									Living After 120 Days
			0	3-5	6-8	9-11	12-16	17-25	31-60	61-90	91-120	
650	Filter	54	...	3	1	16	12	3	3	7	6	3
	No filter	39	3	5	6	12	9	3	...	...	...	...
1,300	Filter	18	...	6	6	4	2	...	...	...	...	...
	No filter	20	...	12	7	1	...	...	...	...	...	...
1,950	Filter	16	...	12	3	1	...	...	...	...	...	...
	No filter	16	...	16	...	...	...	...	...	...	...	...

TABLE II: EFFECT OF IRRADIATION IN SPLENECTOMIZED ANIMALS

X-Ray Dosage (r)	Filtering	Treatment following Splenectomy Days	Number of Animals	Mortality During Post-Irradiation Days									Living After 120 Days
				0	2-5	6-8	9-11	12-14	20-22	42-60	61-90	91-120	
650	Filter	10-15	31	2	2	...	...	...	2	4	3	2	16
	No filter	4-15	32	3	2	...	9	1	6	3	1	...	7
1,300	Filter	14-18	17	...	3	...	5	9	...	...	...	...	...
	No filter	15-18	17	...	7	6	4	...	...	...	...	...	...
1,950	Filter	15	18	...	2	13	3	...	...	...	...	...	...
	No filter	25	18	...	18	...	...	...	...	...	...	...	...

itoneally). The operation was performed through a pararectal incision in the left upper quadrant of the abdomen.

Irradiation was usually administered fifteen days postoperatively. The group irradiated after only four days showed a conspicuous number of deaths in the first forty-eight hours, suggesting that the animals were not yet recovered from the operative stress. Animals of the same age and weight were selected for each group of experiments.

The animals which died at the various intervals after irradiation, as well as the survivors, which were killed after 120, 180, and 190 days, were autopsied and the organs were fixed for histological study.

#### RESULTS

The results obtained will be divided in two general groups: the first is concerned with the normal animals submitted to filtered and unfiltered x-rays; the second with the splenectomized animals. The mortality rate of the normal guinea-pigs is

shown in Table I. For 54 animals receiving 650 r filtered whole-body irradiation we observed a survival rate of 35.1 per cent after twenty and thirty days; 29.6 per cent after sixty days; 16.6 per cent after ninety days; 5.5 per cent after one hundred twenty days. For the animals submitted to filtered x-ray irradiation the maximum mortality incidence was between nine and sixteen days for those receiving 650 r, between five and twelve days for those receiving 1,300 r, and between five and eight days when 1,950 r was given.

The 75 normal guinea-pigs submitted to unfiltered irradiation all died during the first twenty-five days; with 650 r the maximum incidence in mortality was between nine and fourteen days; with 1,300 r between five and seven days; with 1,950 r on the fourth day. In all the animals of the first general group a direct proportionality is observed between dosage and mortality: the higher the x-ray dosage the earlier the death.

In Table II the data on the splenectomized guinea-pigs submitted to whole-body irradiation are reported. Just as in the preceding general group it was observed: (a) that there was a proportional increase in mortality rate with increase in dose; (b) that the filtered rays are less dangerous than the unfiltered ones. The most striking

observation, however, was that splenectomy had a tremendous protective action against x-ray injuries, especially with exposures to relatively low dosage. Of 31 guinea-pigs submitted to 650 r filtered radiation, 80.6 per cent were living after thirty days; 67.7 per cent after sixty days; 51.6 per cent after one hundred twenty days; the survivors were killed after one

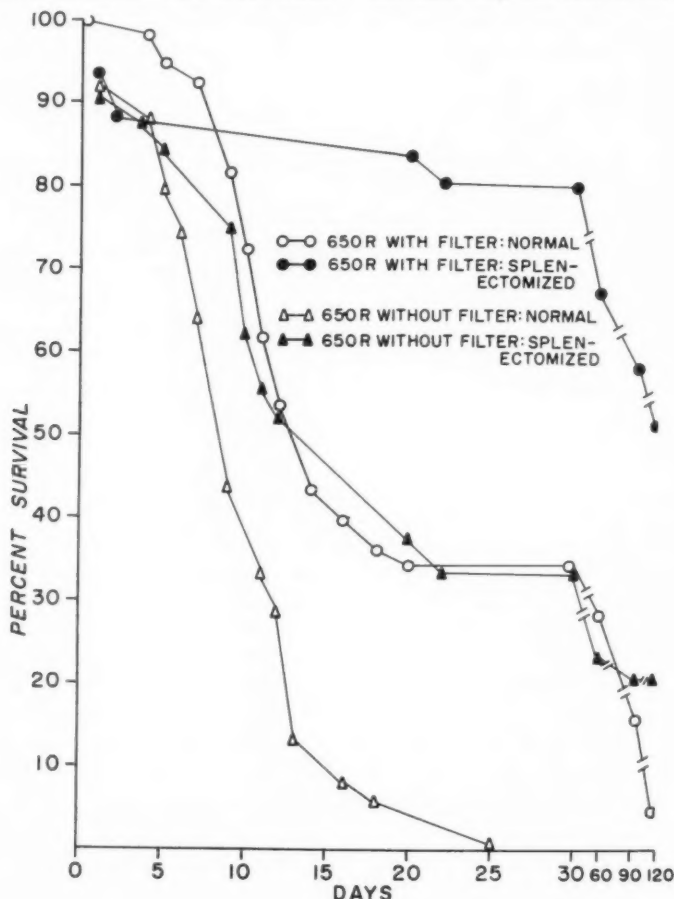


Figure 1

submitted to the same treatment was living). After one hundred twenty days 21.8 per cent of the splenectomized group were still in good health.

The protective action of the splenectomy is graphically demonstrated in Figure 1, which shows the survival curves for normal and splenectomized animals submitted to 650 r, filtered and unfiltered.

hundred eighty and one hundred ninety days. Only 5.6 per cent of the normal animals submitted to the same x-ray treatment were living after one hundred twenty days. Of the 32 splenectomized guinea-pigs submitted to 650 r unfiltered rays 34.3 per cent were living after twenty-five days (on the same day not one of the normal animals

## DISCUSSION

The different biological effects observed in comparative experiments in the two general groups of guinea-pigs, normal and splenectomized, must be considered in relation to the quality of x-ray treatment. It is obvious that the filtered x-rays must have a less severe biological effect than the unfiltered rays.

The patterns of daily deaths, as a function of time after irradiation, are directly related to dosage, and our results are perfectly in agreement with those of Cronkite (29).

The observations on the protective action of splenectomy, which has not before been demonstrated, are in disagreement with those of Raventos (27), who found the postirradiation mortality slightly higher in splenectomized animals than in controls. But the differences between his groups are in any event not statistically significant.

It is generally agreed that acute x-ray injuries are a consequence of two main kinds of effect: (a) alterations in hematopoietic tissue (spleen and bone marrow in particular); (b) alterations of the gastrointestinal epithelium (Fishler *et al.*, 30). After low dosages of x-ray, alterations occur in the hematopoietic tissue only, and these are correlated with the second peak of deaths following x-ray treatment; the first peak is correlated with the irreversible gastrointestinal damage. These considerations explain why the shielding of spleen (18-26, 31) or of other tissues—head (24, 25), liver (24, 25), adrenals (32)—or treatment with bone marrow and spleen homogenate (35-38), by fostering a hematopoietic recovery, are able to enhance the survival of the treated animals. But this protection occurs only when there is no gastrointestinal alteration, *i.e.*, only when low doses of x-rays are employed.

The protective action of hypoxia (39, 42) and of other measures reducing cellular oxygen concentration, *e.g.*, cysteine (40, 43), glutathione (41), must be explained on the ground that x-ray irradiation produces a tremendous amount of free oxidant radicals which are responsible for

the hematopoietic alterations (33, 34).

The protective action of splenectomy, as demonstrated in the studies reported here, can be explained on the basis of the suggestion by Jacobson that irradiation of spleen may so alter it that it functions as a pathological organ, and as a consequence by some humoral mechanism suppresses hematopoietic regeneration. This means that by splenectomy the formation in the spleen of a toxic agent is prevented.

## SUMMARY

A total of 295 normal and splenectomized guinea-pigs were submitted to filtered and unfiltered x-rays generated by a 180 to 200-kv machine, in doses of 650, 1,300, and 1,950 r.

The biological effects differed with different qualities of radiation.

Splenectomy had a definite protective action against x-ray injuries. This protective effect was greater against the lower dosages.

NOTE: We extend our sincere appreciation to Prof. C. Bazzicalupo for his kindly interest and assistance in this work.

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SUMMARIO IN INTERLINGUA

Roentgeno-Irradiation del Corpore Total e Splenectomia in Porcos de India

Cento trenta-tres porcos de India es-  
seva splenectomisate e subsequentemente  
subjicite a roentgeno-irradiation del cor-  
pore total a varie nivellos de dosage, e  
163 porcos de India esseva irradiate sin  
effectuation antecedente de splenectomia.  
In ambe gruppos de animales il esseva  
constatate que filtration modificava le  
effecto lethal del irradiation. Esseva  
etiam notate que le distribution del  
mortes de die in die esseva relationate al  
nivello del dosage. Tamen, le plus frap-  
pante observation esseva que splenec-

tomia habeva un tremende effecto pro-  
tectori contra le injurias de radios X,  
specialmente in le caso de exposition a  
relativemente basse doses. Es opinat  
que iste effecto protectori se explica super  
le base del suggestion de Jacobson que le  
irradiation es capace a alterar le splen in  
un tal maniera que illo functiona como un  
organo pathologic e que per consequente,  
per le un o le altere mechanismo humoral,  
illo supprime le regeneration hemato-  
poietic. Splenectomia preveni assi le for-  
mation de un agente toxic in le splen.



## The Adaptation of Air Chutes to Roentgen Diagnostic Departments<sup>1</sup>

ROY R. GREENING, M.D., and RALPH LOVELIDGE

**N**EWER, RAPID processing methods have demanded that we review our thinking about the organization and design of roentgen diagnostic departments. With the increasing economic pressures in a large, active department, we must critically examine our methods of film matching, reporting, and filing, so that there is less delay between the time of examination and the final roentgen report. Many times, speed in this respect may be life-saving and certainly it may shorten the period of hospitalization and save valuable time for the ambulatory patient.

A second important factor to be considered arises with the newer developing units. This is the location of the dark room. It is no longer necessary that this be in the center of the radiology department. If one could find a means of rapid transport of roentgenograms from any portion of the hospital (operating rooms, receiving wards, out-patient clinics, etc.) these could be sent quickly and efficiently to one central processing center and returned completely processed and ready for reporting and filing.

With this in mind, we reviewed numerous conveyor belt systems, but all of these proved expensive and complicated if there were many corners to be turned or any appreciable distance to be covered. This method, therefore, is not too practical, though it can be used if expense is no item. Many hospitals today make use of air chutes for dispatching records to and from a central record room. Similar chutes, with slight variation, can be used to send roentgenograms anywhere in the hospital, and at reasonable cost. Only standard equipment is necessary, such as has been used for some years in printing houses to send sets of proof to different parts of a



Fig. 1. Standard air-chute container and plastic film-wrapping jacket.

large plant. No special design is necessary, though an extra air compressor may be required in addition to the one in general use in the hospital.

A standard sized container of 14 in. inside length (16 in. outside) can be obtained commercially. The films may be rolled in a black plastic sheath (the container can be coated with black paint but the plastic sheath with enclosed films is easier to insert and remove from the tube than is the rolled film alone), placed in the tube, and sent to a central processing room in a matter of minutes from any department in the modern hospital. The film can be quickly processed (six minutes from dry film to dry film) and returned *via* the chute to its source, whether this

<sup>1</sup> From the Department of Radiology, Hospital of the University of Pennsylvania. Accepted for publication in October 1958.

be one of the operating rooms or a general radiographic room.

At first, we were somewhat apprehensive about the production of artefacts due to rolling of the film and the production of static by changes in moisture content in the air, but with the co-operation of Eastman Kodak Co., utilizing their special climate control and varying the moisture content and temperature, we have found no static as a result of either handling the film or its long journey in the chute under

a variety of climatic conditions. Dr. Morgan at Johns Hopkins Hospital has rolled films and transported them manually in containers for many years without the production of artefacts.

This method of rapid, relatively inexpensive film transport is feasible and practical and may prove of value in the design of newer radiology departments.

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#### SUMMARIO IN INTERLINGUA

##### Communication Pneumatic, Adaptate al Uso per Departimentos Roentgeno-Diagnostic

Un ordinari systema de communication pneumatic, del typo usate pro expedir documentos hospitalari a e ab le archivos central, es proponite pro le transporto de clichés roentgenographic a un station central de tractation ab non importa qual departamento del hospital. Le exponite pellicula es rolate in un vaina de plastic negro e inserite in un receptaculo de dimensiones standard pro le transporto in le

systema pneumatic. Le tractate pellicula pote esser retornate in le mesme maniera.

Con le application de appropriate methodos de regulation de temperatura e humiditate, nulle artefactos ha essite producite, e nulle difficultate ha resultate ab le accumulation de cargas electric in consequentia del manipulation del pellicula e de su viage a transverso le systema pneumatic.



# A Simple Device for Obtaining Lateral Acetabular Views of the Hip in Infants<sup>1</sup>

DONALD B. DARLING, M.D.

THE ACETABULAR lateral view of the hip has considerable usefulness in orthopedic work in infants, especially in cases of congenital dislocation. It is difficult, however, to get comparable projections of both hips routinely, and with the usual method someone must stand in the direct x-ray beam during the exposure. The method to be described not only eliminates irradiation to personnel but makes it easier to obtain satisfactory pictures.

## METHOD

The base is placed on the table and the box set into the track. With its arms held behind its head by means of cotton stockinet, the infant is placed on the box and secured by the compression band. A cassette is inserted into the slot and the buttocks are brought into contact with the cassette. The lower extremities are put into the frog lateral position and placed to encircle the cassette. A Flexi-cast is then laid over the feet and legs and hardened

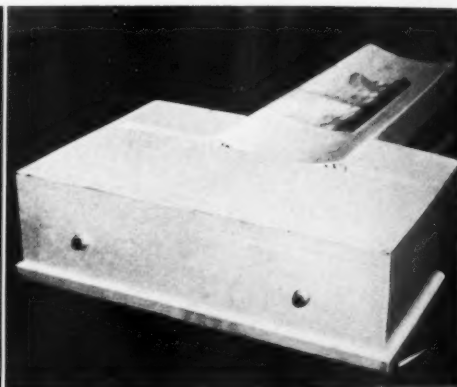
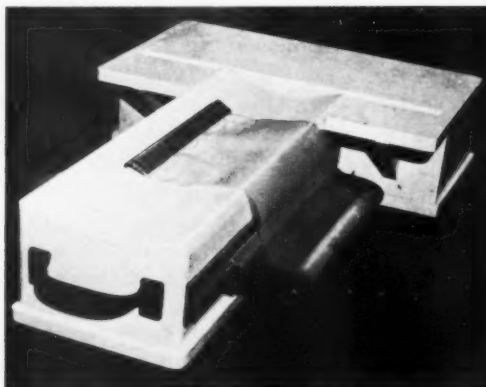


Fig. 1. The acetabular box.

The device is a modification of the acetabular box used elsewhere. Basically it is made in the form of the letter "T" with a slot across the top into which a cassette can be inserted vertically. Side rails are attached to the base of the "T" so that a compression band can be used and an extension of the "T" above the slot makes it possible to immobilize the legs and feet in a Flexi-cast (Fig. 1). A separate base on which a circular track is mounted permits the acetabular box to be rotated 360° on three large ball bearings which are attached to the box and fit onto the track (see arrow, Fig. 2).

to hold them in position (or sandbags may be used). The infant is now safely immobilized and the final positioning is done.

The radiographic tube is placed horizontally at the head of the table and moved down to the level of the hip. An adjustment in the cross table travel of the tube brings the centering light to the hip of interest. The final adjustment is made with one technician sighting down the tube and instructing the other technician to rotate the box on the circular track until the central beam is directed along the inguinal crease between the abdomen and thigh (Fig. 2).

<sup>1</sup> From the Department of Radiology, Children's Hospital of Pittsburgh, and the Department of Radiology, University of Pittsburgh, School of Medicine. Accepted for publication in October 1958.



Fig. 2. Acetabular box in use. The base with the circular track is clearly shown. Note that no personnel are in the room.

A view of the opposite hip is then taken by replacing the exposed cassette with a new one, rotating the box to bring the hip into line with the tube, and making an adjustment of the tube so that the geometrical arrangement duplicates that used on the first side.

The device is simple to use and results in uniformly good and reproducible radiographs as well as completely eliminating personnel exposure in the examination.

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#### SUMMARIO IN INTERLINGUA

#### Un Simple Dispositivo pro le Obtention de Expositiones Latero-Acetabular del Coxa de Infantes

Es describe un dispositivo que permette le obtention de plus satisfacente expositiones del coxa de infantes con dislocation congenite. Il se tracta de un modification del cassa acetabular, construite in le forma del littera T, con un fissura trans le tecto pro le insertion de un cassetta, con rails lateral que permette le uso de un banda de compression, e con un

extension in que es placiante un "Flexi-Cast" pro immobilisar le gambas. Le cassa es montate con cossinettos de ballas super un via circular que permette su rotation per 360 grados.

Iste apparatusa es facile a usar, resulta in uniformemente bon e reproducibile roentgenogrammas, e evita completamente le exposition del personal.



# EDITORIAL

## Forty-Fifth Annual Meeting The Radiological Society of North America

The Radiological Society of North America will hold its Forty-Fifth Annual Meeting at the Palmer House, Chicago, Nov. 15-20, presenting a program which promises to be of interest and value to all. The central theme will be "The Future of Radiology," and papers for presentation, refresher courses, scientific and commercial exhibits are all being planned in that vein. It is hoped that many will be able to be present throughout the week, since the program will reach a climax at the final session, Friday morning, when the newest and most outstanding aspects in the development of our specialty will be considered.

On Sunday afternoon, Nov. 15, the first of the series of Refresher Courses arranged by John W. Walker, M.D., and his committee will open the meeting. The long-time favorite "therapy experts" will start the ball rolling. A second course will be conducted during the late afternoon, followed in the evening by the popular and highly educational Film Interpretation Session. A series of courses on a wide variety of subjects is scheduled for each morning thereafter. It is important that members utilize the opportunity offered elsewhere in this journal to register early for these courses, as only thus can one be sure of attaining his first choice. By the time of registration at the meeting, most of the refresher courses except those conducted in the Ballroom and the Red Lacquer Room will be "sold out." Unfortunately the size and limited number of the rooms make it impossible to take care of everyone who might like to attend a given course. Those courses which are known to be over-subscribed are usually given the larger rooms. Residents in Radiology, trainees

in physics, interns, and medical students will be assured of accommodations in the Ballroom and Red Lacquer Room, and should there be any vacant space at the time of a particular course in a smaller room, these young and interested persons will be accommodated. *It remains important for members to register in advance if they wish to attend a specific refresher course.*

The Scientific Exhibits will, as usual, represent many varied interests, filling the space available for this purpose to capacity. It is to be noted that much material submitted for the scientific program which could not be included will be presented in exhibit form. This has been admirably accomplished through the unending activity of the excellent Chairman of the Scientific Exhibits Committee, Everett L. Pirkey, M.D.

John H. Gilmore, M.D., has continued to serve as Chairman of the Commercial Exhibits Committee, and he has assured us of another outstanding demonstration of new developments in this field.

As in other years, papers have been invited from the membership, and the response has been gratifying. The only unfortunate aspect of the method is that many have had to be refused because of limitations imposed by the general theme of the program and the shortness of the time. It is with great regret that the Program Committee has had to turn down some excellent presentations. Efforts have been made to include as many of these as possible in the Scientific Exhibits or in Refresher Courses. It is indeed rewarding to recognize the amount of advanced thinking going on in the radiologic profession as indicated by the vast amount of material reviewed by the Program Committee.

Certain innovations are planned, and it is believed that these will be unusual and worthwhile. On Wednesday and Thursday mornings a separate section, Section C, arranged by John Hale, Ph.D., will be devoted to papers concerning radiologic physics, paralleling Sections A and B. Section C, "Work in Progress," prepared by Warren Sinclair, Ph.D., will hold its usual Wednesday afternoon place and will also be directed toward the physicists. A clinical "Work in Progress" Section is scheduled for Friday morning, when it is anticipated that the latest and most forward-looking projects in both diagnosis and therapy will be presented. In each field a group of seven-minute papers stressing recent research in radiology will be presented. This is considered by the Program Committee as scintillating material which no radiologist can afford to miss.

The Carman Lecture, Thursday evening, will be followed by the presentation of the Gold Medal of the Society as well as the awards for Scientific Exhibits and the induction of the new officers. We are indeed fortunate this year to have as the Carman Lecturer, Chester M. Jones, M.D., whose work has been closely allied with that toward which Russell Carman directed a lifetime of activity. We are highly honored in having such an outstanding Carman Lecturer.

As always, the local committees have

generously come forward and given their full co-operation in arranging this meeting. Through the years they have continued to contribute largely to these outstanding occasions. I am deeply grateful not only to them for their extreme co-operation and interest, but also to the Women's Committee, with Mrs. John H. Gilmore and Mrs. Earl E. Barth as Co-Chairmen, for arrangement of the ladies program. I should also like to express my gratitude to all of the speakers, the counselors, the officers, and the members of various committees, especially of the Program Committee, for the remarkable help which they have given me in planning this meeting. I have, as is the usual custom, enlisted the able assistance of Donald S. Childs, M.D., and his wonderful assistant, Mrs. Marguerite H. Henry. To them I am deeply grateful.

It is because of the combined efforts of these and many others that this Forty-Fifth Annual Meeting of the Radiological Society of North America cannot fail to carry on the fine traditions of our organization as an educational force for the development of new ideas in scientific radiology. Its fulfillment of this promise will be a recognition of your eager co-operation. All of you, as members or guests, are urged to make a real effort to be in Chicago Nov. 16-21.

LAURENCE L. ROBBINS, M.D.

*President*

## Massive Osteolysis

Osteolysis can be due to a great variety of causes, some of them well known, such as infection, tumors, the reticuloses, trauma (Sudeck's atrophy), various chronic diseases such as rheumatoid arthritis and gout, diseases of the nervous system, hyperparathyroidism, and many others. At rare intervals there have been reported cases in which one or more bones seemed to melt away and vanish more or less completely without known cause. The persons affected are usually children or

young adults in good health. In most instances the disease progresses until one or more of a group of bones have wholly or partially vanished, after which the condition stabilizes and remains unchanged indefinitely. Very rarely it has resulted in death. The bones most frequently involved include those of the upper and lower extremities, the shoulder girdle with adjacent ribs and vertebrae, and the pelvic girdle.

The first case reported was described in

the *Boston Medical & Surgical Journal* in 1838 and again in 1872 as "a boneless arm." The humerus in a young man gradually vanished, beginning at the age of eighteen. The process stabilized and at autopsy at the age of seventy only the upper and lower extremities of the humerus remained. Subsequent sporadic case reports indicated that usually more than one contiguous bones were affected. Trauma often called attention to the condition but did not seem to be a cause and, after assuring themselves that none of the other ordinary causes of osteolysis was responsible, the authors reported themselves baffled both as to etiology and the mechanism of the process. Only rarely were biopsies made, and these were reported as showing nothing significant. It was sometimes noted that the tissue was richly vascular, but no attention was paid to this until Gorham encountered two cases in which vascular proliferation played a dominant role.

Gorham's cases were published in 1954. He noted that vascular proliferation had been observed in a case reported by King in 1946 and that the process had been described by Stout as hemangiomatosis. In this first paper Gorham called attention to the suggestion of increased vascularity in some of the reported cases and he determined to obtain sections from other reporters so that the role of vascular proliferation in the causation of massive osteolysis could be more fully evaluated. In association with Stout, sections from 8 cases were studied. In all of them the dominant feature was the presence of large numbers of vessels in the atrophic bone or in the fibrous tissue occupying the site of the vanished bone. Usually but not invariably the vessels contained red blood cells.

The process was unlike that caused by ordinary angiomas, which tend to be isolated formations and produce limited destruction of bone rather than massive osteolysis. Following the publication of this joint study in 1955, 5 additional cases have been reported, 3 in England and 1 each in Czechoslovakia and the United States. In each instance the authors confirm Gorham and Stout's conception of the disease.

Although the pathological process producing massive osteolysis appears well established, the etiology remains entirely obscure and the mechanism whereby the bone is caused to disappear remains baffling. It would seem that, whereas a rich vascular supply is essential for bone proliferation, in this disease it has an opposite effect. It is beyond the scope of this editorial to discuss this aspect, but it may be remarked that Gorham is at present engaged in an experimental study of the problem. ARTHUR PURDY STOUT, M.D.

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# RADIOLOGICAL SOCIETY OF NORTH AMERICA

## FORTY-FIFTH ANNUAL MEETING: PRELIMINARY PROGRAM

Palmer House, Chicago, Illinois

Nov. 15-20, 1959

Monday, November 16

OPENING SESSION: 1:45-4:30 P.M.

### SECTION AB

Grand Ballroom

Call to Order. LAURENCE L. ROBBINS, M.D., President.  
Greetings. GEORGE C. TURNER, M.D., President,  
Chicago Medical Society.

Benjamin Felson, M.D., Cincinnati, Ohio  
First Vice-President, Presiding

President's Address. LAURENCE L. ROBBINS, M.D.,  
Boston, Mass.

Memorial Fund Lecture: Logical Analysis in Roentgen  
Diagnosis. LEE B. LUSTED, M.D., Rochester, N. Y.  
Introduced by EUGENE P. PENDERGRASS, M.D.

Medicine's Role in Prepaid Medical Care Plans and  
Insurance. L. W. LARSON, M.D., Bismarck, N. D.

Veterinary Radiology: Disease Conditions in Animals,  
with Radiological Findings That Are Also Present in  
Man. STUART A. PATTERSON, M.D., and WILLIAM  
D. CARLSON, PH.D., Denver, Colo.

Aspects of Radiation Research and the Relief of Cancer.  
J. ROBERT ANDREWS, M.D., Bethesda, Md.

BUSINESS MEETING: 4:30 P.M.

Tuesday, November 17

SECTION A: 10:30 A.M.-12:10 P.M.

Grand Ballroom

H. Milton Berg, M.D., Bismarck, N.D.  
Chairman, Board of Directors, Presiding

Psoriatic Arthritis. DAVID G. PUGH, M.D., ROGELIO  
AVILA, M.D., CHARLES H. SLOCUMB, M.D., and  
RICHARD K. WINKELMANN, M.D., Rochester, Minn.

Roentgenographic Time-Lapse Studies of Living Bone.  
III. Consideration of Growth, Rickets, and Bone  
Repair. HOWARD J. BARNHARD, M.D., Philadelphia,  
Penna., F. DIXON CONLIN, M.D., and ROBERT W.  
GEYER, M.D., Little Rock, Ark.

The Number and Distribution of Roentgenologic Ex-  
aminations for 100,000 People. REYNOLD F. BROWN,  
M.D., JOHN M. HESLEP, Ph.D., and WILLIAM S.  
EADS, M.D., San Francisco, Calif.

Some Factors Influencing the Dose Rate from Diag-  
nostic X-ray Apparatus. E. DALE TROUT, D.Sc.,  
JOHN P. KELLEY, B.S., and ARTHUR C. LUCAS, B.S.,  
Milwaukee, Wis.

SECTION B: 10:30 A.M.-12:30 P.M.

Red Lacquer Room

Henry S. Kaplan, M.D., San Francisco, Calif., Presiding

Introduction. HENRY S. KAPLAN, M.D.

Cellular Aspects of Tumor Therapy. MORTIMER M.  
ELKIND, Ph.D., Bethesda, Md.

Oxygen Tension in Malignant Neoplasms. MICHEL  
TER-POGOSSIAN, Ph.D., St. Louis, Mo.

Consequences in Mice of the Continuous Ingestion of  
Sr<sup>90</sup>. MIRIAM FINKEL, Ph.D., PATRICIA J. BERG-  
STRAND, B.S., BIRUTE R. BISKIS, M.D., Lemont, Ill.

Quantitative and Qualitative Evaluation of Skin  
Erythema. ARVIN S. GLICKSMAN, M.D., FLORENCE  
C. H. CHU, M.D., HARRY N. BANE, M.D., and  
JAMES J. NICKSON, M.D., New York, N. Y.

Experimental Evaluation of Radiation Quality.  
FREDERICK J. BONTE, M.D., and J. S. KROHMER,  
M.A., Dallas, Texas.

SECTION AB: 2:00-4:30 P.M.

Grand Ballroom

Theodore J. Wachowski, M.D., Wheaton, Ill.  
President-Elect, Presiding

A Seven-Year Evaluation of the Treatment of Hyper-  
thyroidism with Radioactive Iodine. SIDNEY  
RUBENFELD, M.D., ANTHONY KOHN, M.D., MARTIN  
LOWENTHAL, M.D., NATHAN MITCHELL, M.D., and  
S. STEVEN BRODIE, Ph.D., New York, N. Y.

Pulmonary Veins in Rheumatic Heart Disease.  
ROBERT S. ORMOND, M.D., and ANDREW J. POZNAN-  
SKI, M.D., Detroit, Mich.

Roentgenographic Manifestations of Pulmonary Tula-  
remia. COL. WILLIAM D. TIGERTT, M.C., and LIEUT.  
COL. EDWIN L. OVERHOLT, M.C., U.S.A., Washing-  
ton, D. C.

Some Factors Affecting Response of Lungs to Irradi-  
ation. WILLIAM T. MOSS, M.D., FRANCIS J. HADDY,  
M.D., and STANFORD K. SWEANY, M.D., Chicago.

The Role of Irradiation in the Treatment of Liposar-  
coma and Hemangiopericytoma. MILTON FRIED-  
MAN, M.D., and JOHN W. EGAN, M.D., New York.

Werner's Syndrome: A Clinical-Roentgen Entity.  
HAROLD G. JACOBSON, M.D., HAROLD RIFKIN, M.D.,  
and DOROTHEA ZUCKER-FRANKLIN, M.D., New York.

Tumor Localization with Transverse Tomography:  
Diagnostic and Therapeutic Application. BERNARD  
ROSWIT, M.D., and SOL M. UNGER, M.D., New York.

BUSINESS MEETING: 4:30 P.M.

**Wednesday, November 18****SECTION A: 10:30 A.M.-12:10 P.M.****Grand Ballroom****Charles M. Gray, M.D., Tampa, Fla., Presiding**

The Renal Functions Explored by Cineradiography in Dogs and Rabbits. A Preliminary Study for Investigating Human Renal Functions by Cinenephroangiography. **FRANK L. CAMPETI, M.D., Rochester, N. Y.**

Gastroduodenal X-ray Diagnosis: A Comparison of Radiographic Technics and Interpretations. **LEWIS E. ETTER, M.D., JAMES P. DUNN, M.D., ADOLPH G. KAMMER, M.D., LESLIE H. OSMOND, M.D., and LEWIS C. REESE, M.D., Pittsburgh, Penna.**

Cineradiographic Studies of the Pharynx Following Laryngopharyngeal Surgery. **JAMES J. SCATLIFF, M.D., JOHN A. KIRCHNER, M.D., and DONALD P. SHEDD, M.D., New Haven, Conn.**

The Cinefluorographic Detection and Recording of Calcifications in the Heart. **JOSEPH JORGENSEN, M.D., Minneapolis, Minn.**

Aortic Configuration in Congenital Heart Disease. **JOHN A. CAMPBELL, M.D., and EUGENE C. KLATTE, M.D., Indianapolis, Ind.**

**SECTION B: 10:30 A.M.-12:10 P.M.****Red Lacquer Room****Robert P. Barden, M.D., Philadelphia, Penna., Presiding**

A Comparative Study of the Use of Percutaneous Splenic Portography and Photoscintigraphy in the Demonstration of Liver Disease. **GUENTHER A. DOEHNER, M.D., JOHN C. POWERS, M.D., FRANCIS F. RUZICKA, JR., M.D., and HEINRICH WASHMUTH, M.D., New York, N. Y.**

Experimental Radiation Therapy of Tumors Using  $I^{131}$  Carrying Antibodies to Fibrin. **WILLIAM F. BALE, Ph.D., RUTH L. GOODLAND, M.S., and IRVING L. SPAR, Ph.D., Rochester, N. Y.**

Electron Beam Therapy in the Management of Carcinoma of the Breast. **FLORENCE C. H. CHU, M.D., JORGE L. GASPER-LANDERO, M.D., JAMES J. NICKSON, M.D., and ALAN C. SCHEER, M.D., New York, N. Y.**

Treatment of Malignant Neoplasms in the Thoracic Cage with High-Energy Electrons. **ERICH M. UHLMANN, Chicago, Ill.**

Multisection Transverse Tomography in Radium Implant Calculations. **ROBERT L. EGAN, M.D., and GORDON C. JOHNSON, M.D., Houston, Texas.**

**SECTION C: 10:30 A.M.-12:20 P.M.****Crystal Room****John Hale, Ph.D., Philadelphia, Penna., Presiding**

Design and Performance of Field-Defining Apertures for Neutron Capture Therapy. **E. E. STICKLEY, Ph.D., and L. E. FARR, M.D., Upton, L. I., N. Y.**

A Technic for Large-Field, Superficial Electron Therapy. **C. J. KARZMARK, Ph.D., R. LOEVINGER, Ph.D., R. E. STEELE, Ph.D., and M. WEISSBLUTH, Ph.D., Stanford, Calif.**

Dose Distribution Using a New Scanning Beam Technic for High-Energy Electron Therapy. **LESTER S. SKAGGS, Ph.D., LAWRENCE H. LANZI, Ph.D., and ALICE L. MCCREA, S.M., Chicago, Ill.**

The Physical Characteristics of a Short-Distance Cesium-137 Teletherapy Unit. **W. K. SINCLAIR, Ph.D., A. COLE, Ph.D., and G. H. FLETCHER, M.D., Houston, Texas.**

Assessment of the Radiation Dose Due to Fallout. **PHILIP F. GUSTAFSON, Ph.D., Lemont, Ill.**

**SECTION AB: 2:00-5:00 P.M.****Grand Ballroom****Richard H. Chamberlain, M.D., Philadelphia, Penna., Presiding**

Panel on Bone Marrow Transplants and General Immunological Problems:

Some Experiences with Irradiation Injury. **JOSEPH W. FERREBEE, M.D., and E. DONNALL THOMAS, M.D., Cooperstown, N. Y.**

A Comparison of the Effects of Isologous, Homologous and Heterologous Hematopoietic Tissues on Postirradiation Survival. **LEON O. JACOBSON, M.D., Chicago, Ill.**

The Theory and Practice of Total-Body Irradiation in the Dawn of the Homograft Era. **JAMES B. DEALY, JR., M.D., Boston, Mass.**

Physical Considerations in the Whole-Body Irradiation of Man. **EDWARD W. WEBSTER, Ph.D., Boston, Mass.**

Complications of Selective Angiocardiography. **JEAN L. HERDT, M.D., and THEODORE F. HILBISH, M.D., Bethesda, Md.**

Selective Angiography of the Left Heart, Aorta, and Coronary Arteries. **CHARLES T. DOTTER, M.D., Portland, Ore.**

Coronary Arteriography in Man. **CHARLES V. MECKSTROTH, M.D., WILLIAM MOLNAR, M.D., and SIDNEY W. NELSON, M.D., Columbus, Ohio.**

**SECTION C: 2:00-5:00 P.M.****Crystal Room**

**Recent Advances in Radiologic Physics,**  
**W. K. Sinclair, Ph.D., Houston, Texas, Presiding**

This program is arranged only a few weeks before the meeting, and details are therefore not now available.

**Thursday, November 19****SECTION A: 10:30 A.M.-12:10 P.M.****Grand Ballroom****William R. Eyler, M.D., Detroit, Mich., Presiding**

The Roentgen Diagnosis of Acoustic Tumors. **SAMUEL B. HAVESON, M.D., Los Angeles, Calif., and ALFRED L. SCHMITZ, M.D., San Francisco, Calif.**



Pathways of Cerebral Collateral Circulation. MAURICE TATELMAN, M.D., Detroit, Mich.  
 Primary Intraventricular Tumors. ROBERT P. BOUDREAU, M.D., Baltimore, Md.  
 Increased Intracranial Pressure: Roentgen Studies in Adults. SIDNEY P. TRAUB, M.D., Saskatoon, Sask.  
 Uranium X-ray Grids. MICHEL TER-POGOSSIAN, Ph.D., St. Louis, Mo.

#### SECTION B: 10:30 A.M.-12:10 P.M.

##### Red Lacquer Room

Jesshill Love, M.D., Indianapolis, Ind., Presiding

Microwave Studies in Progress. HERBERT MERMAGEN, Rochester, N. Y.  
 Leukemia Induced by Radiation: A Study of Survivors of Radium-Treated Cancer of the Uterine Cervix. MARSHALL BRUCER, M.D., RAYMOND HAYES, M.D., and NORMAN SIMON, M.D., Oak Ridge, Tenn.  
 Incidence of Neoplasia Following Irradiation of Children for Nonmalignant Diseases. EUGENE L. SAENGER, M.D., FREDERIC N. SILVERMAN, M.D., THEODORE STERLING, Ph.D., Cincinnati, Ohio, and MALCOLM TURNER, M.A., Richmond, Va.  
 Nasopharyngeal Malignant Tumors: 74 Consecutive Patients Treated in a Period of 21 Years. JEROME M. VAETH, M.D., San Francisco, Calif.  
 Pre-operative Radiation in the Treatment of Cancer of the Esophagus. EUGENE L. BRONSTEIN, M.D., EUGENE E. CLIFFTON, M.D., JOHN T. GOODNER, M.D., and OMAR HUSTA, M.D., New York, N. Y.

#### SECTION C: 10:30 A.M.-12:30 P.M.

##### Crystal Room

Gail D. Adams, Ph.D., San Francisco, Calif., Presiding

Wedge Filters: Their Design, Fabrication, and Use in Megavoltage Radiation Therapy. STANLEY E. SNEIDER, M.D., HERMAN D. SUIT, M.D., ROBERT W. SWAIN, B.S., and J. ROBERT ANDREWS, M.D., Bethesda, Md.  
 Exit Dosimeter for Effective Patient Thickness. R. G. WOODLEY, M.S., EUGENE L. BRONSTEIN, M.D., and J. S. LAUGHLIN, Ph.D., New York, N. Y.  
 Problems of Developing a Film Method for Regularly Checking Radiation Output of X-Ray Therapy Machines. LEONARD STANTON, M.S., Philadelphia.  
 A Comprehensive Radiation Control Program in New York City. HANSON BLATZ, New York, N. Y.

#### SECTION AB: 2:00-4:30 P.M.

##### Grand Ballroom

Russell H. Morgan, M.D., Baltimore, Md., Presiding

Some Biomedical Problems of the Atomic Age. CHARLES L. DUNHAM, M.D., Washington, D. C.

Radiation Exposure on Nuclear Submarines. LIEUT. COMDR. JOHN H. EBERSOLE, M.C., USN, Washington, D. C.

Radiation in the Environment of the Earth. ERNEST C. RAY, Ph.D., Iowa City, Iowa.

Gastric Carcinoma: Accuracy of Radiologic Diagnosis. ROBERT D. MOSELEY, JR., M.D., NELS M. STRANDJORD, M.D., and RAYMOND L. SCHWEINEFUS, B.S., Chicago, Ill.

Upper Gastrointestinal Tract Alterations in Adenomatosis of the Endocrine Glands. RALPH SCHLAEGER, M.D., New York, N. Y., MARJORIE LEMAY, M.D., Boston, Mass., and PAUL WERMER, M.D., New York, N. Y.

The Value of Emergency Intravenous Cholangiography in the Differential Diagnosis of Acute Cholecystitis. HENRY C. JOHNSON, JR., JOHN R. McLAREN, M.D., and H. STEPHEN WEENS, M.D., Atlanta, Ga.

Midgut Volvulus. R. PARKER ALLEN, M.D., DAVID R. AKERS, M.D., and CHARLES E. SHOPFNER, M.D., Denver, Colo.

#### BUSINESS MEETING: 4:30 P.M.

#### THE CARMAN LECTURE: 8:30 P.M.

##### Grand Ballroom

Laurence L. Robbins, M.D., Boston, Mass.  
 President, Presiding

The Carman Lecture: Malnutrition Secondary to Impaired Intestinal Absorption. CHESTER M. JONES, M.D., Boston, Mass.

Presentation of the Gold Medal of the Society.

Announcement of the Scientific Awards.

Introduction of New Officers.

Presentation of the Pfahler Gavel.

#### Friday, November 20

#### SECTION A: 10:30 A.M.-12:30 P.M.

##### Grand Ballroom

Work in Progress: Recent Advances in Diagnosis  
 David S. Carroll, M.D., Memphis, Tenn., Presiding

This program is arranged only a few weeks before the meeting, and details are therefore not available for publication here.

#### SECTION B: 10:30 A.M.-12:30 P.M.

##### Red Lacquer Room

Work in Progress: Recent Advances in Therapy  
 Alfred M. Popma, M.D., Boise, Idaho, Presiding

This program is arranged only a few weeks before the meeting, and details are therefore not available for publication here.

## REFRESHER COURSES: POSTGRADUATE INSTRUCTION

The 1959 Refresher Course Series will be presented during the Forty-Fifth Annual Meeting of the Radiological Society of North America at the Palmer House, Chicago, Ill. Registration for the meeting will begin at 1:00 P.M., Saturday, Nov. 14. On Sunday, Nov. 15, the registration desk will be open at 9:00 A.M.; it will be open at 8:00 A.M. Monday through Friday. *Please register early.* The courses will start at 2:00 P.M. Sunday, Nov. 15, with the Therapy Information Session. This will be followed by a second course, on Radiation Protection, from 4:30 to 5:30, and the Film Reading Session at 7:00 P.M.

Due to the popularity of the refresher courses and the great demand for tickets, new courses have been added, to be held in new rooms at the Palmer House.

On Monday, Nov. 16, there will be a series of courses beginning at 8:30 A.M. and continuing until 10:00 A.M., with a second series from 10:30 A.M. until 12:00. The remainder of the week the Refresher Course period will be from 8:30 to 10:00 A.M. No other meetings will be scheduled during these hours. Attendance is limited to the medical profession, including graduate students and residents in radiology, radiation physicists, radiobiologists, chemists, medical students certified by the deans of their respective medical schools, and others closely allied with the science of radiology. Residents, interns, and medical students will be limited to courses being presented in the Grand Ballroom and the Red Lacquer Room, unless unlimited space is available in other courses.

A registration fee of \$25.00, which includes the refresher course fee, must be paid by all nonmembers of the Radiological Society of North America at the time of registration at the Palmer House. The excep-

tions are guest speakers, guest instructors, scientific exhibitors, residents or fellows in radiology, medical students, trainees in physics, and officers in the Armed Forces of the United States on temporary duty away from their practice. Members of the Radiological Society of North America are not required to pay a registration fee or a refresher course fee. All must register at the R.S.N.A. desk in the Palmer House. Payment of the registration fee by nonmembers is *not* to accompany the request for tickets, but is to be paid at the time of registration. All refresher course tickets will be held for you at the registration desk at the Palmer House. Please call for them there.

Admission to the courses will be by presentation of the registration badge and a ticket for the particular course, except for Courses Nos. 1, 2, and 3 on Sunday. Admission to these three courses will be by badge only. If you cannot use the tickets you have reserved, please notify the Chairman of the Refresher Course Committee.

Read the description of the courses, noting particularly the days on which they are offered, and make your selection for the day. Turn to the colored insert, indicate thereon your first, second, and third choice for the day, and mail the request promptly. The number attending each course is limited by the capacity of the room in which it is held, and *requests for tickets will be filled in the order in which they are received.* You will be notified regarding your selection of courses.

We would appreciate suggestions for future courses, as well as for new instructors for some of the present ones. Please put your suggestions on a card and leave it at the registration desk, or mail it directly to the Refresher Course Chairman.

### Course No. 1: Sunday, 2:00-4:00 P.M.

#### Therapy Information Session

MILTON FRIEDMAN, M.D., New York, N. Y.  
Moderator

M. M. KLIGERMAN, M.D., New Haven, Conn.  
ROBERT ROBBINS, M.D., Philadelphia, Penna.  
J. W. J. CARPENDER, M.D., Chicago, Ill.

A series of selected cases will be presented showing the clinical course of the lesion, pathology, and results. Only histologically proved cases will be used.

### Course No. 2: Sunday, 4:30-5:30 P.M.

#### Radiation Protection

RICHARD H. CHAMBERLAIN, M.D.,  
Philadelphia, Penna.  
Moderator

PHILIP J. HODES, M.D., Philadelphia, Penna.  
TED F. LEIGH, M.D., Atlanta, Ga.  
JOHN HALE, Ph.D., Philadelphia, Penna.

A movie entitled "Radiation: Physician and Patient" will be shown, followed by a panel discussion. Audience participation is invited.

### Course No. 3: Sunday, 7:00-9:00 P.M.

#### Film Interpretation Session

JOHN A. EVANS, M.D., New York, N. Y.  
Moderator

JOHN F. HOLT, M.D., Ann Arbor, Mich.  
BENJAMIN FELSON, M.D., Cincinnati, Ohio  
LESTER W. PAUL, M.D., Madison, Wisc.

This session is a diagnostic symposium based on proved cases. Every effort will be made to present cases that are of educational value, and that will

permit an orderly, analytical approach to a diagnostic problem.

Any member of the Radiological Society who wishes to contribute an instructive case may submit his material to the Moderator, John A. Evans, M.D., The New York Hospital-Cornell Medical Center, 525 East 68th Street, New York 21, N. Y.

#### Course No. 4: Monday, 8:30-10:00 A.M.

##### Treatment Planning: Conventional Energy X-Rays

A. RAVENTOS, M.D., and JOHN HALE, Ph.D.  
Philadelphia, Penna.

Deep-seated lesions as well as superficial lesions can be treated adequately with stationary x-ray beams generated at 250 kvp or less. Realization of the full potentialities of conventional x-ray therapy, particularly for deep-seated lesions, often requires careful treatment planning based upon a good practical knowledge of the physical principles involved. In this course, the basic principles of treatment planning will be discussed from the standpoint of both physics and clinical practice, and some of the methods that have proved useful will be outlined. Some clinical examples requiring the use of very low, intermediate, and 250-kvp x-ray beams will be discussed in detail.

#### Course No. 5: Monday, 8:30-10:00 A.M.

##### Gynecological and Obstetrical Radiology

K. C. CORLEY, M.D., and FRED O. COE, M.D.  
Washington, D. C.

Discussion will cover three main subjects:

1. Hysterosalpingography.
2. Pelvimetry.
3. Recognition of abnormal pelvic soft-tissue masses.

Films or slides will demonstrate findings in the three categories and technics will be described. No discussion of therapy will be included.

#### Course No. 6: Monday, 8:30-10:00 A.M.

##### Pulmonary Embolism

FELIX G. FLEISCHNER, M.D.  
Boston, Mass.

Starting with the pathogenesis and roentgen diagnosis of the pulmonary infarct, the discussion will emphasize the diagnosis of pulmonary embolism without infarct formation, including pleural effusion, inhibited respiration, and the roentgen signs of acute and chronic cor pulmonale.

#### Course No. 7: Monday, 8:30-10:00 A.M.

##### Radiology of the Urinary Tract

JOHN A. CAMPBELL, M.D.  
Indianapolis, Ind.

Interpretation of roentgen studies of the urinary

tract requires an understanding of the basic embryologic, anatomic, physiologic, and pathologic factors involved. In addition, the indications, limitations, and specific usefulness of the various methods of radiologic investigation of the urinary tract structures should be fully appreciated.

Illustrative case material will be used to demonstrate the roentgen signs of various types of upper urinary tract diseases according to different pathologic and functional categories. The findings will be analyzed as to their technical dependence, specificity, and application to differential diagnosis.

##### Period I

- (a) Technic of radiologic examination.
- (b) Normal variants and significant anomalies.
- (c) Obstructive lesions.

##### Period II

- (a) Infections and calculi.
- (b) Retroperitoneal mass lesions.
- (c) Trauma.

(This course continued Tuesday, Course No. 36)

#### Course No. 8: Monday, 8:30-10:00 A.M.

##### Neuroradiology

ALFRED L. SCHMITZ, M.D.  
Los Angeles, Calif.

Bone changes in meningiomas, acoustic nerve tumors, and sellar tumors will be discussed. The technic and the normal roentgen anatomy in fractional encephalography will be illustrated. Normal encephalograms will be compared with those showing changes in the ventricular system and cisterns secondary to tumor pathology. Cerebral arteriograms will be presented to augment the encephalographic studies.

(This course continued Tuesday, Course No. 33)

#### Course No. 9: Monday, 8:30-10:00 A.M.

##### Colon: Symposium on Technic of Examination

GEORGE A. MILLER, M.D., Urbana, Ill.  
Moderator

ALFRED O. MILLER, M.D., Louisville, Ky.  
LEO S. FIGIEL, M.D., Grosse Point, Mich.  
CHARLES W. YATES, M.D., Houston, Texas  
LAWRENCE A. DAVIS, M.D., Louisville, Ky.

This course will be a Symposium on the use of various technics in the examination of the colon, including the image intensification, high-voltage technic, high-voltage spot-film technic, double air-contrast enemas, and special problems in the examination of the infant.

#### Course No. 10: Monday, 8:30-10:00 A.M.

##### Basic Radiation Dosimetry

H. O. WYCKOFF, Ph.D.  
Washington, D. C.

The text for the course is the 1959 Recommendations of the International Commission on Radio-

logical Units and Measurements.<sup>1</sup> The difference between the exposure dose in roentgens, the absorbed dose in rads, and the RBE dose in rems will be pointed out. Data on energy dependence and rate dependence of r-meters will be presented, and suggestions will be made on methods for checking the reproducibility of such instruments. Direct measurement of the absorbed dose by calorimetric means will be discussed, but the principal method considered will be the computation of absorbed dose from ionization measurement.

<sup>1</sup> Revision of NBS Handbook 62.

**Course No. 11: Monday, 8:30-10:00 A.M.**

**Intravenous Cholangiography**

ROBERT E. WISE, M.D.  
Boston, Mass.

Five years experience with over two thousand injections for cholangiography will be presented. Pitfalls and diagnostic criteria of organic biliary tract disease, with emphasis on the post-cholecystectomy patient, will be considered. Although the procedure has been of great value in confirming the presence of organic disease, its greater value may lie in exclusion, thus preventing needless surgery.

**Course No. 12: Monday, 8:30-10:00 A.M.**

**Radiology and Health Insurance: Some Questions and Answers**

WILLIAM C. STRONACH  
Chicago, Ill.

A systemic disease of the health insurance industry, characterized by a high fever with insistence upon hospital bed occupancy as the basis for the insurance coverage of radiology, compels a treatment of choice which will allow the patient the advantage of x-ray coverage without being driven into a hospital bed to obtain it.

The cure is insurance of ambulatory patients, rather than bed patients only, this *medical* insurance—as opposed to *hospital* insurance—to be available either in the radiologist's office or his outpatient department in a hospital.

Contents of this course will be presented through use of the case history method. The course content will describe the problem of radiologic coverage as seen in such socio-economic arenas as Cleveland, Buffalo, Philadelphia, and Kansas City.

The testimony of instructors in the course will emphasize not only "how we did it," but also "how you can do it too" procedures—and whether, in individual circumstances, these procedures failed or succeeded and why. Emphasis will be on the answers, documents, and data which will be useful in obtaining x-ray coverage in medical insurance contracts to the advantage of the patient, the insurance agency—be it profit or nonprofit—the hospital, and the radiologist.

Arranged through co-operation with the American

College of Radiology current insurance education program, this course will attempt to illustrate with pragmatic, empirical evidence how radiology for nonbed patients in medical insurance contracts is good medicine, good insurance, good economics, and good sense.

**Course No. 13: Monday, 8:30-10:00 A.M.**

**Radiotherapy of Carcinoma of the Skin**

JUAN A. del REGATO, M.D.  
Colorado Springs, Colo.

Although cell sensitivity may account for a small percentage of failures in treatment of carcinoma of the skin, most failures are due to the selection of improper technic. A plan of treatment for various skin lesions will be given.

**Course No. 14: Monday, 8:30-10:00 A.M.**

**Metabolic and Endocrine Diseases Involving the Skeletal System**

HOWARD L. STEINBACH, M.D.  
San Francisco, Calif.

The major endocrine and metabolic factors affecting growth and maturation, and some recent concepts of the dynamic aspects of bone composition, physiology, and pathology, will be discussed. To be considered are the radiologic aspects of the more common metabolic diseases, such as osteoporosis and osteomalacia, and the unusual manifestations of these diseases. The second part of the discussion will deal with endocrine abnormalities producing skeletal alterations, recognizable by roentgenographic methods.

(This course continued Tuesday, Course No. 30)

**Course No. 15: Monday, 10:30-12:00 A.M.**

**Basic Electronics for Radiologists**

LOUIS H. FRISCHE, M.D., and  
CHARLES T. DOTTER, M.D.  
Portland, Ore.

Electronic complexities have made appraisal of modern equipment increasingly difficult for the practicing radiologist, beleaguered as he is by other professional responsibilities. The objective of this course, therefore, is to review elementary principles, emphasizing everyday radiological applications. Operation of power supply, simple vacuum tubes, electronic switches, and similar devices will be discussed, supplemented by practical demonstration.

(This course continued Tuesday, Course No. 27)

**Course No. 16: Monday, 10:30-12:00 A.M.**

**Radiology of the Larynx and Pharynx**

ARNOLD L. BACHMAN, M.D.  
New York, N. Y.

This course includes radiographic anatomy and

physiology of the larynx, radiology of laryngeal paralysis, radiology of normal and abnormal swallowing patterns, tumors of the larynx and pharynx, and demonstration of extension of laryngopharyngeal tumors. In addition, certain benign conditions will be discussed, including foreign bodies of the cervical esophagus, cricopharyngeal spasm and radiology of the adenoids.

(This course continued Tuesday, Course No. 28)

#### Course No. 17: Monday, 10:30-12:00 A.M.

##### Therapeutic Uses of Isotopes

ROBERT ROBBINS, M.D., Philadelphia, Penna.

Moderator

EUGENE L. SAENGER, M.D., Cincinnati, Ohio

JOHN P. STORAASLI, M.D., Cleveland, Ohio

ROBERT HASTERLIK, M.D., Chicago, Ill.

The members of the panel will discuss common therapeutic applications of isotopes, on the basis of their own experience and opinions. It is hoped that the session will be based entirely on questions and problems posed by members of the audience as arising in their practice and experience in the use of therapeutic isotopes. The panel members will endeavor to give practical assistance and advice on these problems.

#### Course No. 18: Monday, 10:30-12:00 A.M.

##### Translumbar Aorto-arteriography

OWINGS W. KINCAID, M.D.

Rochester, Minn.

The aims, technical problems, and various methods of aortography and femoral arteriography via the aorta will be reviewed. More emphasis will be placed on the study of vascular occlusive disease than on renal artery study. The technic and results of the method currently employed at the instructor's institution will be reviewed in detail. Stress will be placed on the importance of visualizing the femoral arteries during aortography, and a method of doing so. Correlation between the roentgenologic appearances, functional impairment, and surgical considerations will be discussed.

#### Course No. 19: Monday, 10:30-12:00 A.M.

##### Prognostic Significance of Some of the Secondary Metastases of Lung Cancer

GWILYM S. LODWICK, M.D.

Columbia, Mo.

This course will present experiences in the study of clinical data, roentgenograms, and survival statistics from 542 cases of lung cancer. These data have been compiled and studied by technics similar to those used with a collection of bone sarcomas, and comparisons and parallel conclusions will be drawn from both series. Roentgen prognostic signs of poor and long survival will be illustrated.

#### Course No. 20: Monday, 10:30-12:00 A.M.

##### Radiotherapy in Ophthalmology

GEORGE R. MERRIAM, JR., M.D.

New York, N. Y.

The use of radiation in the treatment of ocular lesions will be discussed, with particular attention to the late effects. The clinical course of various diseases will be described briefly and the anticipated benefits of irradiation evaluated in terms of other therapeutic measures and the possible late sequelae. The discussion will be divided into three categories: superficial, low-voltage, and high-voltage therapy. The factors, dose, treatment time, and technic for each condition will be considered.

Under *superficial therapy*, both grenz rays and beta radiation will be considered, and the treatment of such conditions as vernal catarrh, corneal vascularization, precancerous melanosis, recurrent pterygia, nodular episcleritis, phlyctenular keratitis, bullous and filamentary keratitis, and resistant corneal ulcers will be covered.

The *low-voltage therapy* discussion will concern primarily the treatment of epithelization of the anterior chamber. A brief discussion of the relative values of radiation and surgery in basal- and squamous-cell carcinoma of the lid will be presented.

Under *high-voltage therapy* such lesions as retinoblastoma, ocular lymphosarcoma, orbital hemangiomas, and metastatic carcinoma of the eye and orbit, will be covered.

#### Course No. 21: Monday, 10:30-12:00 A.M.

##### Male Cystourethrography

NATHANIEL FINNEY, M.D., New York, N. Y.

and

ALBERT J. PAQUIN, M.D., Charlottesville, Va.

Methods and technics of cystourethrography will be presented, with a demonstration of normal anatomy and physiology and their variants. The radiology of congenital and acquired diseases of the bladder and urethra will be demonstrated by cystourethrograms. Periurethral calcification and prostatic disease will also be discussed.

(This course continued Tuesday, Course No. 34)

#### Course No. 22: Monday, 10:30-12:00 A.M.

##### Radiographic Examination of the Upper Gastrointestinal Tract

WENDELL P. STAMFELI, M.D.

Denver, Colo.

The technic of radiographic examination of the esophagus, stomach, and duodenum will be very briefly reviewed. This will be followed by a presentation of case material emphasizing the common as well as some of the more unusual lesions of the stomach and duodenum encountered in a large private hospital practice.



# PLAN OF PRESENTATION

SUNDAY, Nov. 15 2:00-4:00 P.M.	MONDAY, Nov. 16 8:30-10:00 A.M.	MONDAY, Nov. 16 10:30-12:00	TUESDAY, Nov. 17 8:30-10:00 A.M.
<p><b>1. Therapy Information Session</b> Milton Friedman, M.D., Moderator M. M. Kligerman, M.D. Robert Robbins, M.D. J. W. I. Carpenter, M.D.</p> <p>4:30-5:30 P.M.</p> <p><b>2. Radiation Protection</b> Richard H. Chamberlain, M.D., Moderator Philip J. Hodes, M.D. Ted F. Leigh, M.D. John Halle, Ph.D.</p> <p>7:00-9:00 P.M.</p> <p><b>3. Film Interpretation Session</b> John A. Evans, M.D., Moderator John F. Holt, M.D. Benjamin Felson, M.D. Lester W. Paul, M.D.</p>	<p><b>4. Treatment Planning: Conventional Energy X-Rays</b> A. Raventos, M.D. John Hale, Ph.D.</p> <p><b>5. Gynecological and Obstetrical Radiology</b> K. C. Corley, M.D. Fred O. Coe, M.D.</p> <p><b>6. Pulmonary Embolism</b> Felix G. Fleischner, M.D.</p> <p><b>7. Radiology of the Urinary Tract (Cont. Tuesday)</b> John A. Campbell, M.D.</p> <p><b>8. Neuroradiology (Cont. Tuesday)</b> Alfred L. Schmitz, M.D.</p> <p><b>9. Colon: Symposium on Technic</b> George A. Miller, M.D., Moderator for Alfred O. Miller, M.D., Leo S. Figiel, M.D. Charles W. Yates, M.D., Lawrence A. Davis, M.D.</p> <p><b>10. Basic Radiation Dosimetry</b> H. O. Wyckoff, Ph.D.</p> <p><b>11. Intravenous Cholangiography</b> Robert E. Wise, M.D.</p> <p><b>12. Radiology and Health Insurance: Some Questions and Answers</b> William C. Stronach</p> <p><b>13. Radiotherapy of Carcinoma of the Skin</b> Juan A. del Regato, M.D.</p> <p><b>14. Metabolic and Endocrine Diseases Involving the Skeletal System (Cont. Tuesday)</b> Howard L. Steinbach, M.D.</p>	<p><b>15. Basic Electronics for Radiologists (Cont. Tuesday)</b> Louis H. Frische, M.D. Charles T. Dotter, M.D.</p> <p><b>16. Radiology of the Larynx and Pharynx (Cont. Tuesday)</b> Arnold L. Bachman, M.D.</p> <p><b>17. Therapeutic Uses of Isotopes</b> Robert Robbins, M.D., Moderator Eugene L. Saenger, M.D. John P. Storaasli, M.D. Robert Hasterlik, M.D.</p> <p><b>18. Translumbar Aorto-arteriography</b> Owings W. Kincaid, M.D.</p> <p><b>19. Prognostic Significance of Some of the Secondary Manifestations of Lung Cancer</b> Gwilym S. Lodwick, M.D.</p> <p><b>20. Radiotherapy in Ophthalmology</b> George R. Merriam, Jr., M.D.</p> <p><b>21. Male Cystourethrography (Cont. Tuesday)</b> Nathaniel Finby, M.D. Albert J. Paquin, M.D.</p> <p><b>22. Radiographic Examination of the Upper Gastrointestinal Tract</b> Wendell P. Stampfli, M.D.</p> <p><b>23. Selective Destruction of Tissue Components by Intense Ultrasound</b> W. I. Fry, Ph.D.</p> <p><b>24. Respiratory Distress of the Newborn and Infant</b> George Jacobson, M.D. Victor G. Miktly, M.D.</p> <p><b>25. The Physiodynamics of Respiration</b> W. Walter Wasson, M.D.</p>	<p><b>26. Treatment Planning with High Energy Radiation (Particularly Telecobalt)</b> Lucille A. DuSault, A.B. Robert J. Bloor, M.D.</p> <p><b>27. Basic Electronics for Radiologists (Cont. from Monday)</b> Louis H. Frische, M.D. Charles T. Dotter, M.D.</p> <p><b>28. Radiology of the Larynx and Pharynx (Cont. from Monday)</b> Arnold L. Bachman, M.D.</p> <p><b>29. Therapeutic Uses of Radioisotopes (Dosimetry)</b> W. K. Sinclair, Ph.D.</p> <p><b>30. Metabolic and Endocrine Diseases Involving the Skeletal System (Cont. from Monday)</b> Howard L. Steinbach, M.D.</p> <p><b>31. Diagnostic Applications of Radioactive Isotopes (Cont. Wednesday)</b> John P. Storaasli, M.D. J. S. Krohmer, M.A.</p> <p><b>32. Neutron Dosimetry</b> H. H. Rossi, Ph.D.</p> <p><b>33. Neuroradiology (Cont. from Monday)</b> Alfred L. Schmitz, M.D.</p> <p><b>34. Male Cystourethrography (Cont. from Monday)</b> Nathaniel Finby, M.D. Albert J. Paquin, M.D.</p> <p><b>35. Recent Developments in Radiobiology</b> Titus C. Evans, Ph.D.</p> <p><b>36. Radiology of the Urinary Tract (Cont. from Monday)</b> John A. Campbell, M.D.</p>

**WEDNESDAY, Nov. 18**  
8:30-10:00 A.M.

37. Female Pelvic Cancer (Cont. Thursday)  
Walter T. Murphy, M.D.
38. Treatment Planning in Rotation Therapy  
M. M. Kligerman, M.D.  
E. H. Quimby, D.Sc.
39. Myelography: Technic and Interpretation (Cont. Thursday)  
Sidney P. Traub, M.D.
40. Some Fundamentals in Chest Roentgen Interpretation (Cont. Thursday)  
Benjamin Felson, M.D.
41. Cancer Chemotherapy in Radiological Practice  
Bernard Roswit, M.D.
42. Diagnostic Applications of Radioactive Isotopes (Cont. from Tuesday)  
John P. Storaasli, M.D.  
J. S. Krohmer, M.A.
43. Examination of the Gastrointestinal Tract in Infants and Children  
Lawrence A. Davis, M.D.
44. Dosimetry with Chemical Systems  
N. F. Barr, Ph.D.
45. The Small Intestine (Cont. Thursday)  
Richard H. Marshak, M.D.
46. Mammalian Radiobiology  
I. W. Osborne, Ph.D.  
E. F. Riley, Ph.D.
47. Roentgen Manifestations of Some Diseases of Bones and Joints (Cont. Thursday)  
Harold G. Jacobson, M.D.

**THURSDAY, Nov. 19**  
8:30-10:00 A.M.

48. Dosage in Internal Use of Radium and Other Radioisotopes as Discrete Sources  
Elizabeth F. Focht, B.A.
49. Radiology of Congenital Heart Disease (Cont. Friday)  
John A. Campbell, M.D.  
Eugene C. Klatte, M.D.
50. Studies with  $I^{131}$ -Labeled Proteins  
R. S. Yalow, Ph.D.
51. Some Fundamentals in Chest Roentgen Interpretation (Cont. from Wednesday)  
Benjamin Felson, M.D.
52. The Mediastinum (Cont. Friday)  
Ted F. Leigh, M.D.  
H. Stephen Weens, M.D.
53. Common Causes of Radiation Hazards  
Carl B. Braestrup, B.S., P.E.  
Theodore Eberhard, M.D.
54. The Small Intestine (Cont. from Wednesday)  
Richard H. Marshak, M.D.
55. Female Pelvic Cancer (Cont. from Wednesday)  
Walter T. Murphy, M.D.
56. Bone Marrow Transplantation in Radiation Protection  
V. P. Bond, M.D.
57. Roentgen Manifestations of Some Diseases of Bones and Joints (Cont. from Wednesday)  
Harold G. Jacobson, M.D.
58. Myelography: Technic and Interpretation (Cont. from Wednesday)  
Sidney P. Traub, M.D.

**FRIDAY, Nov. 20**  
8:30-10:00 A.M.

59. The Mediastinum (Cont. from Thursday)  
Ted F. Leigh, M.D.  
H. Stephen Weens, M.D.
60. Applications of Computers to Medical Problems  
R. Taplin, B.S.
61. Radiology of Congenital Heart Disease (Cont. from Thursday)  
John A. Campbell, M.D.  
Eugene C. Klatte, M.D.
62. Instrumentation for Clinical Radiological Physics  
C. S. Simons, Ph.D.
63. Radiotherapy of Carcinoma of the Larynx  
Juan A. del Regato, M.D.
64. Practical Techniques in Pediatric Radiology  
Lawrence A. Davis, M.D.
65. Radiation Exposure and Protection with Various Diagnostic Procedures  
M. L. Meurk, B.S.  
R. S. Sherman, M.D.
66. The Chest in Industry  
Eugene P. Pendergrass, M.D.
67. Genetic Effects of Radiation  
E. F. Oakberg, Ph.D.
68. Radiation Treatment of Carcinoma of the Cervix Uteri  
Edwin C. Ernst, M.D.
69. Bronchography  
William Molnar, M.D.

**Course No. 23: Monday, 10:30-12:00 A.M.****Selective Destruction of Tissue Components by Intense Ultrasound**

W. J. FRY, Ph.D.  
Urbana, Ill.

Intense ultrasound can, under accurately controlled dosage conditions, produce selective changes in tissue. By focusing the radiation it is possible to produce changes at any desired depth without adverse effect on intervening tissue, and by moving the focus of the ultrasonic beam(s) it is possible to irradiate volumes of complex shape and orientation. Irradiation can be accomplished as often as desired since there is no cumulative effect on tissue which the radiation traverses to the sites of the focus.

This lecture will include a discussion of (1) types of selective changes which are induced in tissue by controlled dosages of high-intensity ultrasonic radiation, (2) the techniques and instrumentation which are employed to treat tissue with ultrasonic energy, (3) the present state of knowledge of the physical mechanism of the action of the sound on the tissue, and (4) indicated directions of research in this field for the immediate future. Ultrasonic irradiation of deep brain structures of experimental animals and human beings with neurological disorders will be illustrated with motion pictures.

**Course No. 24: Monday, 10:30-12:00 A.M.****Respiratory Distress of the Newborn and Infant**

GEORGE JACOBSON, M.D.,  
and  
VICTOR G. MIKITY, M.D.  
Los Angeles, Calif.

Roentgenological interpretation in the infant and newborn has often been a perplexing problem. This course will deal with some of the problems of the child with respiratory distress.

**Course No. 25: Monday, 10:30-12:00 A.M.****The Physiodynamics of Respiration**

W. WALTER WASSON, M.D.  
Denver, Colo.

The primary lobule of William Snow Miller is the basic lobule of the lung. It contains three systems: (1) the bronchial system; (2) the vascular system; (3) the lymphatic system. The function of these systems is to some extent controlled by a fourth system—the nervous system. The anatomy of the basic lobule will be presented, together with a discussion of the physiodynamics of this anatomy which has to do with the ventilation and air pressures of the bronchial system, the pulmonary capillary flow, and the lymph flow.

Finally, there will be a brief discussion of the influence of the physiodynamics upon the pattern of disease as seen upon the roentgen film.

**Course No. 26: Tuesday, 8:30-10:00 A.M.****Treatment Planning with High Energy Radiation (Particularly Telecobalt)**

LUCILLE A. Du SAULT, A.B.,  
and  
ROBERT J. BLOOR, M.D.  
Detroit, Mich.

A simplified technic for making treatment plans will be presented. The general principles of treatment planning with high-energy radiation will first be discussed, followed by a presentation of treatment plans chosen for specific clinical problems and the reasons for their choice. Special problems in dosage calculation will be oblique fields, compensating filters, and changes in treatment distance.

**Course No. 27: Tuesday, 8:30-10:00 A.M.****Basic Electronics for Radiologists**

LOUIS H. FRISCHE, M.D.,  
and  
CHARLES T. DOTTER, M.D.  
Portland, Ore.

(Continued from Monday, Course No. 15)

**Course No. 28: Tuesday, 8:30-10:00 A.M.****Radiology of the Larynx and Pharynx**

ARNOLD L. BACHMAN, M.D.  
New York, N. Y.

(Continued from Monday, Course No. 16)

**Course No. 29: Tuesday, 8:30-10:00 A.M.****Therapeutic Uses of Radioisotopes (Dosimetry)**

W. K. SINCLAIR, Ph.D.  
Houston, Texas

The therapeutic use of radioisotopes depends on the deposition of as much radiant energy as possible at the disease site, with the minimum dissipation of energy in healthy tissues elsewhere. Concentration of the radioactive material at the site to be treated must therefore be achieved:

- I. By metabolic accumulation of the isotope.
- II. By the physical nature of the material (colloid).
- III. By deliberate localization of specific sources by intracavitary, interstitial, or superficial means.

The basic principles of dosimetry for  $\beta$ - and  $\gamma$ -radiation will be discussed, with references to particular therapeutic procedures from each of these groups.

**Course No. 30: Tuesday, 8:30-10:00 A.M.****Metabolic and Endocrine Diseases Involving the Skeletal System**

HOWARD L. STEINBACH, M.D.  
San Francisco, Calif.

(Continued from Monday, Course No. 14)

**Course No. 31: Tuesday, 8:30-10:00 A.M.****Diagnostic Applications of Radioactive Isotopes**

JOHN P. STORAASLI, M.D.  
Cleveland, Ohio  
and  
J. S. KROHMER, M.A.  
Dallas, Texas

The most common diagnostic uses of radioactive isotopes will be discussed. The first part of the course will be devoted to the physical requirements and equipment available. The second part will be given over to the various clinical applications of radioisotopes.

Some of the diagnostic uses to be discussed will be as follows:

1. Thyroid function studies including uptakes, clearance rates, PBI'S, and TSH test.
2. Circulation studies, including blood volume, cardiac output, liver flow, and peripheral vascular studies.
3. Body scanning, including thyroid, liver, and blood pools.
4.  $P^{32}$  in the diagnosis of intraocular tumors.
5. Metabolic studies including pancreatic insufficiency studies and assay of "intrinsic factor."

(This course continued Wednesday, Course No. 42)

**Course No. 32: Tuesday, 8:30-10:00 A.M.****Neutron Dosimetry**

H. H. ROSSI, Ph.D.  
New York, N. Y.

The assessment of the physical effect of neutron radiation on biological systems requires not only familiarity with techniques of neutron dosimetry but also an understanding of the physical processes involved when neutrons interact with tissue. A brief summary of these phenomena will be given, with emphasis on neutron attenuation in biological systems. This will be followed by a presentation of basic principles of neutron dosimetry and a discussion of the applications of these principles to practical neutron dosimetry in radiobiology and in radiation protection. The discussion will pertain to the dosimetry of neutrons and mixed radiation fields containing neutrons and gamma rays at three levels of increasing detail:

1. The measurement of the total dose.
2. The separate measurement of the dose due to neutrons and gamma rays.
3. The measurement of dose as a function of linear energy transfer.

**Course No. 33: Tuesday, 8:30-10:00 A.M.****Neuroradiology**

ALFRED L. SCHMITZ, M.D.  
Los Angeles, Calif.

(Continued from Monday, Course No. 8)

**Course No. 34: Tuesday, 8:30-10:00 A.M.****Male Cystourethrography**

NATHANIEL FINBY, M.D.  
New York, N. Y.  
and  
ALBERT J. PAQUIN, M.D.  
Charlottesville, Va.

(Continued from Monday, Course No. 21)

**Course No. 35: Tuesday, 8:30-10:00 A.M.****Recent Developments in Radiobiology**

TITUS C. EVANS, Ph.D.  
Iowa City, Iowa

1. Mechanisms of radiation effects as demonstrated in irradiation studies with ascites tumor cells.
2. The oxygen effect.
3. Bone-marrow and spleen extracts in treatment of radiation injury.
4. Radiation and longevity.
5. The fallout problem from the biologic point of view.
6. Relative effectiveness of different kinds of radiation.

**Course No. 36: Tuesday, 8:30-10:00 A.M.****Radiology of the Urinary Tract**

JOHN A. CAMPBELL, M.D.  
Indianapolis, Ind.

(Continued from Monday, Course No. 7)

**Course No. 37: Wednesday, 8:30-10:00 A.M.****Female Pelvic Cancer**

WALTER T. MURPHY, M.D.  
Buffalo, N. Y.

Discussion will cover technic, end-results, and complications of irradiation of cancer of the uterine cervix, uterine corpus, ovary, vagina, vulva, and urethra.

(This course continued Thursday, Course No. 55)

**Course No. 38: Wednesday, 8:30-10:00 A.M.****Treatment Planning in Rotation Therapy**

M. M. KLIGERMAN, M.D.  
New Haven, Conn.  
and  
E. H. QUIMBY, D.Sc.  
New York, N. Y.

The problem is the determination of dose at points within or at the surface of an irregular volume, when the relative motion of the volume with respect to a beam of radiation is one of rotation.

The procedure for dose determination should be generally applicable, accurate, simple to use, and quick. The use of standard isodose charts, available in any radiotherapy department, allows calculation of dose at points continuously irradiated

within the volume and at points in the volume that receive radiation only during part of the rotation time.

The possibilities of the use of rotation will be presented with examples of the calculations, and material will be distributed to the participants for practice in working out the dose distributions. The calculated values will be compared with experimental values obtained for the same set of factors, as well as with dose distributions obtained using other methods of calculation.

#### Course No. 39: Wednesday, 8:30-10:00 A.M.

##### Myelography: Technic and Interpretation

SIDNEY P. TRAUB, M.D.  
Saskatoon, Canada

###### Part I

1. Brief historical review.
2. Indications and contraindications.
3. Pertinent roentgen anatomy and anatomic variations.
4. Technic.
5. Complications and their significance.
6. Intervertebral disk protrusions
  - (a) Value of chest and spine roentgenograms.
  - (b) Cervical disk protrusions.
  - (c) Thoracic disk protrusions.
  - (d) Lumbar disk protrusions.

###### Part II

1. Postoperative myelogram.
2. Intraspinal tumors:
  - (a) Extradural.
  - (b) Intradural (extramedullary).
  - (c) Intramedullary.
3. Vascular malformations; arachnoiditis; sacral cysts.
4. Oxygen myelogram.
5. Water soluble myelography; discography.
6. Errors and pitfalls in myelographic interpretation.

(This course continued Thursday, Course No. 58)

#### Course No. 40: Wednesday, 8:30-10:00 A.M.

##### Some Fundamentals in Chest Roentgen Interpretation

BENJAMIN FELSON, M.D.  
Cincinnati, Ohio

Chest roentgen interpretation should not merely represent an attempt to correlate particular shadows with specific diseases but should be approached with an understanding of the basic principles of anatomy, physiology, pathology, and radiology involved. Some of these principles will be considered and their practical application illustrated.

###### Period I

1. A method of fluoroscopy.
2. The "silhouette" sign.
3. The air bronchogram.

###### Period II

1. Anatomic variations in the pulmonary fissures.
2. Lobar collapse.
3. Lobar enlargement.
4. The disrupted fissure.

(This course continued Thursday, Course No. 51)

#### Course No. 41: Wednesday, 8:30-10:00 A.M.

##### Cancer Chemotherapy in Radiological Practice

BERNARD ROSWIT, M.D.  
Bronx, N. Y.

Cytotoxins, antimetabolites, antibiotics, and steroids have recently gained great importance as adjuncts to radiation treatment. It is essential that radiologists keep abreast of these new developments to improve their management of patients with advanced cancer. This course has been planned by radiologists for radiologists, to discuss available drugs, dosage, indications, clinical effectiveness, complications, and integration with the radiation treatment as well as the trend of future developments in this field. A Chemotherapy Manual will be distributed.

#### Course No. 42: Wednesday, 8:30-10:00 A.M.

##### Diagnostic Applications of Radioactive Isotopes

JOHN P. STORAASLI, M.D.  
Cleveland, Ohio  
and  
J. S. KROHMER, M.A.  
Dallas, Texas

(Continued from Tuesday, Course No. 31)

#### Course No. 43: Wednesday, 8:30-10:00 A.M.

##### Examination of the Gastrointestinal Tract in Infants and Children

LAWRENCE A. DAVIS, M.D.  
Louisville, Ky.

Examination of the gastrointestinal tract in infants and younger children is difficult only in the technical problems involved. Actually, the range of abnormality is limited and does not compare with the complexity of pathology found in the adult. This course will stress the technical problems and how they can easily be solved by the radiologist and one technician. The various congenital and acquired diseases found in pediatric practice will be analyzed, and the use of water-soluble opaque media discussed.

#### Course No. 44: Wednesday, 8:30-10:00 A.M.

##### Dosimetry with Chemical Systems

N. F. BARR, Ph.D.  
New York, N. Y.

The theory of radiation chemical dosimetry will be



discussed with special reference to clinical and radiobiological applications. Chemical dosimetry will be contrasted with ionization methods and the advantages and limitations stressed with the aid of numerous examples of the use of chemical dosimetry. Early developments in chemical dosimetry will be briefly reviewed and G will be compared with W.

Basic principles of the radiation chemistry of aqueous solutions will be reviewed and their bearing on chemical dosimetry stressed. The behavior of chemical dosimeters in general will be discussed in light of these principles, using the Fricke ferrous sulfate dosimeter as a particular example. Determination of the G value and matching of mean atomic number will be stressed.

The application of the foregoing principles to the development of more sensitive chemical systems will be discussed, with examples of the latter.

Finally, particular examples of the use of chemical dosimeters in a variety of clinical situations such as implant dosimetry, whole body and gonadal dose determinations, R.B.E. studies, depth dose determinations, isotope dosimetry, and dosimetry of mixed radiation fields will be discussed.

#### Course No. 45: Wednesday, 8:30-10:00 A.M.

##### The Small Intestine

RICHARD H. MARSHAK, M.D.  
New York, N. Y.

##### Part I

1. Technic, including a discussion of the various barium preparations.
2. Concepts of small intestinal patterns.
3. The malabsorption syndrome. Sprue, lymphosarcoma and Whipple's disease.
4. Interpretation of functional changes.
5. Barium studies in small intestine obstruction.

##### Part II

1. Regional enteritis.
2. Infarction of the small bowel.
3. Tumors.
4. Miscellaneous disorders including scleroderma, amyloidosis, allergy.

(The course continued Thursday, Course No. 54)

#### Course No. 46: Wednesday, 8:30-10:00 A.M.

##### Mammalian Radiobiology

I. W. OSBORNE, Ph.D., and E. F. RILEY, Ph.D.  
Iowa City, Iowa

##### I. The intestinal syndrome (J. W. Osborne)

- (a) The whole-body irradiation syndrome.
- (b) The "intestinal death."
- (c) Irradiation of the exteriorized intestine.
- (d) Experimental modification of the radiosensitivity of the intestine.

##### II. Radiation cataracts (E. F. Riley)

- (a) Ocular damage from irradiation.
- (b) Ophthalmoscopically and histologically ob-

servable changes leading to lens opacification.

- (c) Relative effectiveness of single exposures to fast neutrons compared with single exposures to x-radiation.
- (d) Relative effectiveness of x- and neutron radiations in multiple exposures.
- (e) The limiting of radiation damage by shielding part of a lens.

#### Course No. 47: Wednesday, 8:30-10:00 A.M.

##### Roentgen Manifestations of Some Diseases of Bones and Joints

HAROLD G. JACOBSON, M.D.  
New York, N. Y.

*The Arthritides and Allied Disorders:* Tuberculosis, rheumatoid arthritis and spondylitis, suppurative arthritis, osteoarthritis, spondylosis deformans, "swayback" syndrome, gout, neuropathic joints, sarcoid, and pigmented villonodular synovitis.

*Miscellaneous Skeletal Abnormalities:* Paget's disease, fibrous dysplasia, leontiasis ossium, caisson worker's aseptic necrosis, Gaucher's disease, skeletal findings in various blood dyscrasias (agnogenic myeloid metaplasia, sickle-cell anemia, Hodgkin's disease leukemia, etc.), osteoid osteoma, the important so-called aseptic necroses in childhood (Köhler's, Kienböck's, Freiberg's, osteochondritis dissecans, osteochondrosis of the spine, Legg-Perthes, etc.), idiopathic coxa vera of childhood, epiphyseolysis of the femoral capital epiphysis, the reticuloses (eosinophilic granuloma, Hand-Christian-Schüller's disease and Letterer-Siwe's disease), hyperparathyroidism, Cushing's syndrome, and hypertrophic pulmonary osteoarthropathy.

A concise but rather complete description of the pathological changes in each of these entities will be presented and the relationship of the pathological findings to the roentgen manifestations will be discussed. The concept of explaining the roentgen findings in terms of the pathologic changes will receive special emphasis.

(This course continued Thursday, Course No. 57)

#### Course No. 48: Thursday, 8:30-10:00 A.M.

##### Dosage in Internal Use of Radium and Other Radioisotopes as Discrete Sources

ELIZABETH F. FOCHT, B.A.  
New York, N. Y.

The principle and technics of dosage calculations in the use of discrete sources for intracavitary or interstitial therapy are similar for all gamma-emitting isotopes. The course this year will concentrate on discrete gamma sources only. The fundamentals of amount, exposure, filter, distribution and resultant dose will be discussed for these sources in general. Different systems of radium dosage evaluation and their recent modifications will be analyzed and adapted to the use of such isotopes as cobalt, gold, iridium, etc., including consideration of the time factor.

Three-dimensional models of some actual seed, needle, and tube distributions will be shown with their radiographs, and the processes of making them will be summarized. Methods of calculation from the radiographs or from the models will be explained.

An outline of the subject will be given, with references, which should afford a survey of the information—and philosophies—to date.

#### Course No. 49: Thursday, 8:30–10:00 A.M.

##### Radiology of Congenital Heart Disease

JOHN A. CAMPBELL, M.D., and  
EUGENE C. KLATIE, M.D.  
Indianapolis, Ind.

The advent of successful open heart surgery has changed the importance of roentgen diagnosis of congenital heart disease from a matter of academic interest to one of practical necessity. The roentgenologist serves several key functions in the diagnosis of the lesions. It is frequently his original fluoroscopic and plain film interpretations which lead to the recognition of these malformations, and distinguish those requiring more specialized diagnostic studies. As a member of the hospital cardiology team, the radiologist provides an indispensable service by performing selective cardioangiographic procedures which yield precise information about the altered morphology and hemodynamics.

This course will present the plain film and cardioangiographic diagnosis of the common types of congenital heart disease. Cineradiographic studies will be used to illustrate the pathologic anatomy and physiology of the different conditions. The differential diagnosis of those lesions producing similar clinical features will be emphasized.

##### Period I

1. Basic considerations in roentgen diagnosis.
2. Patent ductus arteriosus.
3. Ventricular septal defect.
4. Atrial septal defect.
5. Anomalous pulmonary venous return.

##### Period II

1. Coarctation of aorta.
2. Fibroelastosis and myocardial disease.
3. Pulmonary stenosis.
4. Tetralogy of Fallot.
5. Tricuspid atresia.
6. Truncus arteriosus.
7. Transposition of great vessels.
8. Miscellaneous.

(This course continued Friday, Course No. 61)

#### Course No. 50: Thursday, 8:30–10:00 A.M.

##### Studies with $I^{131}$ -Labeled Proteins

R. S. YALOW, Ph.D.  
New York, N. Y.

Methods for the use of  $I^{131}$ -labeled proteins in

studies of protein distribution and metabolism will be discussed with particular reference to albumin- $I^{131}$  and insulin- $I^{131}$  as representative of serum proteins and hormones respectively. Problems associated with  $I^{131}$ -labeling of proteins in general and with labeling at high specific activities in particular will be considered. Factors to be evaluated will include damage incident to chemical procedures and to self-irradiation. Techniques will be described for the detection, measurement, and correction of such alterations in the biological integrity of the labeled proteins. The advantages and pitfalls of  $I^{131}$ -labeled proteins compared to proteins labeled with other isotopes will be presented.

Reference will be made to the diverse applications of  $I^{131}$ -labeled proteins to problems of radiation chemistry, endocrinology, and immunology.

#### Course No. 51: Thursday, 8:30–10:00 A.M.

##### Some Fundamentals in Chest Roentgen Interpretation

BENJAMIN FELSON, M.D.  
Cincinnati, Ohio

(Continued from Wednesday, Course No. 40)

#### Course No. 52: Thursday, 8:30–10:00 A.M.

##### The Mediastinum

TED F. LEIGH, M.D., and H. STEPHEN WEENS, M.D.  
Atlanta, Ga.

The course will cover the following:

1. Anatomy and physiology of the mediastinum.
2. Tumors: of the thymus, thyroid, parathyroids, esophagus, peripheral nervous system, fat, lymph nodes, bone and cartilage and others; teratomas, germinal tumors, mesotheliomas, mesenchymomas; tumors of blood vascular origin, and tumors of lymph vascular origin.
3. Cysts: bronchogenic, digestive tract, pericardial, celomic and inflammatory, thymic, parasitic, and others.
4. Aneurysms: of the aorta, pulmonary artery, other arteries, and the veins.
5. Miscellaneous lesions: abscesses, diaphragmatic herniations, meningoceles, paramedastinal pulmonary lesions, and others.

(This course continued Friday, Course No. 59)

#### Course No. 53: Thursday, 8:30–10:00 A.M.

##### Common Causes of Radiation Hazards

CARL B. BRAESTRUP, B.S., P.E.  
New York, N. Y.  
and  
THEODORE EBERHARD, M.D.  
Ann Arbor, Mich.

The hazards associated with the medical use of roentgen rays and with teletherapy may be minimized by the use of properly constructed equip-

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## REFRESHER COURSES

### THE RADIOLOGICAL SOCIETY OF NORTH AMERICA

*November 15 through November 20, 1959*

PALMER HOUSE  
CHICAGO, ILLINOIS

(Detach here)

SEE INSTRUCTIONS ON REVERSE SIDE

### FILL OUT THE FOLLOWING

(Print or type).....

Last Name

First Name or Initials

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State

### CHECK THE FOLLOWING

Member R.S.N.A. ☐

Guest ☐

Resident or fellow in Radiology at present ☐

Where.....

Medical Student ☐

Where.....

Reserve Officer on Active Duty at present ☐

Trainee in Physics ☐

**Fill out, also, the enrollment diagram on the reverse side of this page**



## INSTRUCTIONS FOR ENROLLMENT

Read the accompanying description of the courses and plan of presentation. Register early; the number admitted to each course will be limited by the seating capacity of the room. Reservations will be made in the order of the receipt of request. Admission to the Refresher Courses will be by badge and tickets except for Courses Nos. 1, 2, and 3, for which only a badge will be required. No tickets will be issued for these sessions.

Courses are limited to the medical profession, including graduate students and residents in radiology; radiation physicists, radiobiologists, chemists, and others closely concerned with the science of radiology; and medical students certified by the deans of their respective colleges.

Residents, interns, and medical students will be limited to courses being presented in the Grand Ballroom and the Red Laquer Room, unless unlimited space is available in other courses.

All tickets will be held for you at the R.S.N.A. Registration Desk in the Palmer House.

The registration fee, where applicable, will cover the cost of the Refresher Courses. Members, guest speakers, guest instructors, scientific exhibitors, residents or fellows in radiology, medical students, members of the Armed Forces, and trainees in physics do not pay a registration fee. Non-members not in these groups will pay, *at the time of registration*, a fee of \$25.00, which will include the Refresher Courses.

*If you cannot attend the course reserved for you, kindly notify the Refresher Course Chairman. The seating capacity is very limited in some of the courses and your notice will allow another to attend.*

## PLEASE INDICATE YOUR FIRST, SECOND AND THIRD CHOICES

Tickets Will Be Picked Up at Time of Registration

	First Choice		Second Choice		Third Choice	
	Course No.	Instructor	Course No.	Instructor	Course No.	Instructor
Monday, Nov. 16 8:30 A.M.						
Monday, Nov. 16 10:30 A.M.						
Tuesday, Nov. 17						
Wednesday, Nov. 18						
Thursday, Nov. 19						
Friday, Nov. 20						

Mail this order sheet to John W. Walker, M.D., Chairman, Refresher Course Committee

Prior to Nov. 7, 830 Argyle Bldg., Kansas City 6, Mo.

After Nov. 7, c/o Radiological Society of North America, Palmer House, Chicago 90, Ill.

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ment, ample room shielding and, most important, appropriate operating procedures. These factors will be discussed from the point of view of the safety of the patient, staff, and public. The subject will be further subdivided into fluoroscopy, radiography, roentgen therapy and teletherapy, with emphasis given to the necessary safeguards of each application.

**Course No. 54: Thursday, 8:30-10:00 A.M.**

**The Small Intestine**

**RICHARD H. MARSHAK, M.D.**  
New York, N. Y.

*(Continued from Wednesday, Course No. 45)*

**Course No. 55: Thursday, 8:30-10:00 A.M.**

**Female Pelvic Cancer**

**WALTER T. MURPHY, M.D.**  
Buffalo, N. Y.

*(Continued from Wednesday, Course No. 37)*

**Course No. 56: Thursday, 8:30-10:00 A.M.**

**Bone Marrow Transplantation in Radiation Protection**

**V. P. BOND, M.D.**  
New York, N. Y.

The possibility of using total-body irradiation and bone-marrow transplants in the therapy of a variety of clinical conditions arose directly from animal radiation protection studies. These studies indicated that shielding of the spleen, or injection of spleen or bone-marrow preparations, afforded significant protection of rodents through accelerated bone-marrow regeneration. Although earlier work indicated the possibility of a humoral agent, actual cell transplantation was later demonstrated.

The resultant stimulation of interest in human marrow transplants was heightened by the demonstration that mouse leukemia might be "cured" by heavy irradiation of animals followed by transplantation of normal marrow to allow survival. Later rejection of marrow has occurred, probably on an antibody reaction basis. Marrow transplants have now been attempted in a number of patients for leukemia, for marrow aplasia, after irradiation and kidney transplantation, and for victims of reactor accidents. These experiences will be discussed in terms of clinical indications, transplantation techniques, the type of donor necessary, possible preservation of marrow, evidence for successful transplantation, and possible transplant rejection or other delayed effects.

The doses of radiation used will be discussed in terms of the levels at which survival is possible with "supportive measures" only (antibiotics, transfusions, platelets), and the levels at which transplants may be successful and may allow survival.

**Course No. 57: Thursday, 8:30-10:00 A.M.**

**Roentgen Manifestations of Some Diseases of Bones and Joints**

**HAROLD G. JACOBSON, M.D.,** New York, N. Y.

*(Continued from Wednesday, Course No. 47)*

**Course No. 58: Thursday, 8:30-10:00 A.M.**

**Myelography: Technic and Interpretation**

**SIDNEY P. TRAUB, M.D.**  
Saskatoon, Canada

*(Continued from Wednesday, Course No. 39)*

**Course No. 59: Friday, 8:30-10:00 A.M.**

**The Mediastinum**

**TED F. LEIGH, M.D., and H. STEPHEN WEENS, M.D.**  
Atlanta, Ga.

*(Continued from Thursday, Course No. 52)*

**Course No. 60: Friday, 8:30-10:00 A.M.**

**Applications of Computers to Medical Problems**

**R. TAPLIN, B.S.,** Nutley, N. J.

Statistical analysis of medical problems has been greatly simplified by the use of rapid computers. The types of machines will be discussed and their application to medical problems will be shown.

**Course No. 61: Friday, 8:30-10:00 A.M.**

**Radiology of Congenital Heart Disease**

**JOHN A. CAMPBELL, M.D.,**  
and  
**EUGENE C. KLATTE, M.D.**  
Indianapolis, Ind.

*(Continued from Thursday, Course No. 49)*

**Course No. 62: Friday, 8:30-10:00 A.M.**

**Instrumentation for Clinical Radiological Physics**

**C. S. SIMONS, Ph.D.,** Ann Arbor, Mich.

From the standpoint of using readily available commercial instruments, this course will review some practical methods of determining for the use of the radiation therapist the following information:

- (a) Exposure dose and exposure dose rate.
- (b) Absorbed dose and absorbed dose rate.
- (c) Half-value layer.
- (d) Central axis depth dose value.

In addition, the use of portable monitoring equipment will be considered in performing radiation surveys of therapy installations, comprising

- (a) Teletherapy units.
- (b) Deep therapy units.
- (c) Superficial therapy units.

A listing of the minimum essential equipment for use in a hospital physicist's office will be presented and discussed.

Radioisotope instrumentation will not be treated.

#### Course No. 63: Friday, 8:30-10:00 A.M.

##### Radiotherapy of Carcinoma of the Larynx

JUAN A. del REGATO, M.D.  
Colorado Springs, Colo.

A plan of radiotherapy will be given for cancer of the larynx. It will be shown how the technic must vary with involvement of the perilyngeal structures.

#### Course No. 64: Friday, 8:30-10:00 A.M.

##### Practical Technics in Pediatric Radiology

LAWRENCE A. DAVIS, M.D.  
Louisville, Ky.

The various technics successfully used in radiography and fluoroscopy in children will be demonstrated and discussed. Stress will be placed on simplicity and radiation protection. The technics used in gastrointestinal examination, excretory urography, and cardiac fluoroscopy will be detailed.

#### Course No. 65: Friday, 8:30-10:00 A.M.

##### Radiation Exposure and Protection with Various Diagnostic Procedures

M. L. MEURK, B.S., and R. S. SHERMAN, M.D.  
New York, N. Y.

A review of the radiation safety recommendations and requirements for diagnostic radiological installations will be presented. Methods for minimizing the dose to patients and to radiological personnel will be discussed. Dose figures are obtained from measurements made by the instructors and those reported in the literature.

#### Course No. 66: Friday, 8:30-10:00 A.M.

##### The Chest in Industry

EUGENE P. PENDERGRASS, M.D.  
Philadelphia, Penna.

There will be a brief discussion of the etiology

and pathology of silicosis. Some of the difficulties encountered in the differential diagnosis will be emphasized. A few cases illustrating the medico-legal aspects will be discussed.

#### Course No. 67: Friday, 8:30-10:00 A.M.

##### Genetic Effects of Radiation

E. F. OAKBERG, Ph.D.  
Oak Ridge, Tenn.

The discussion will deal primarily with the induction of mutations by radiation in both male and female mice and will include the effect of gametogenic stage on type and frequency of mutations obtained, mutation frequency at different dose rates, the shape of the mutation rate curves with both acute and chronic exposure, the spectrum of effects of radiation-induced mutations, the high frequency of recessive lethals, the semi-dominant effects of some mutations, and possible interpretations of the lower mutation rate with chronic exposure. These data will be discussed in relation to previous data obtained on *Drosophila* and to the problem of genetic hazards of radiation in man.

#### Course No. 68: Friday, 8:30-10:00 A.M.

##### Radiation Treatment of Carcinoma of the Cervix Uteri

EDWIN C. ERNST, M.D.  
St. Louis, Mo.

The clinical and technical treatment approach, together with a practical discussion of the advantages and disadvantages of the various radiation therapy methods employed in this country and abroad, will be presented, and the results compared in the light of more recent radium dosage research investigations.

#### Course No. 69: Friday, 8:30-10:00 A.M.

##### Bronchography

WILLIAM MOLNAR, M.D.  
Columbus, Ohio

A simple technic of bronchography will be discussed, and a series of cases will be shown correlating the findings with the gross pathology.

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## ANNOUNCEMENTS AND BOOK REVIEWS

### AMERICAN BOARD OF RADIOLOGY

The Spring 1960 examination will be held at the Terrace Hilton Hotel, Cincinnati, Ohio, June 6-10. The deadline for filing applications is Jan. 1, 1960.

A Special Examination in Nuclear Medicine for diplomates in Radiology or Therapeutic Radiology will be offered, provided there are sufficient applications.

H. DABNEY KERR, M.D., *Secretary*

### BUFFALO RADIOLOGICAL SOCIETY

Recently elected officers of the Buffalo Radiological Society are: Charles Bernstein, M.D., President; Casimir Jenczeski, M.D., Vice-President; Alfred Dobrak, M.D., Sisters of Charity Emergency Hospital, Buffalo 4, N. Y., Secretary; Sawyer Glidden, M.D., Batavia, Treasurer.

### SECTION ON RADIOLOGY OF MEDICAL SOCIETY OF DISTRICT OF COLUMBIA

The officers of the Section on Radiology of the Medical Society of the District of Columbia for 1959-60 are: President, George Tievsky, M.D.; Vice-President, Charles E. Bickham, Jr., M.D.; Secretary-Treasurer, William E. Sheely, M.D., 1746 K St., N. W., Washington 6, D. C.

### LOS ANGELES RADIOLOGICAL SOCIETY

Recently elected officers of the Los Angeles Radiological Society are as follows: Putnam C. Kennedy, M.D., President; Robert E. Rickenberg, M.D., Vice-President; Robert B. Engle, M.D., Treasurer; Denis C. Adler, M.D., 2010 Wilshire Blvd., Los Angeles 57, Secretary; Lewis J. Peha, M.D., Member of Executive Committee for three years.

The Society meets the second Wednesday of September, November, March, April, and June, in the Los Angeles County Medical Association Building.

### MAINE RADIOLOGICAL SOCIETY

The Maine Radiological Society has elected the following officers for the ensuing year: President, John F. Gibbons, M.D., Portland; Vice-President, Francis J. O'Connor, M.D., Augusta; Secretary-Treasurer, Edward C. Porter, M.D., Eastern Maine General Hospital, Bangor; Councilor to the American College of Radiology, George E. C. Logan, M.D., Portland.

### OHIO STATE RADIOLOGICAL SOCIETY

Officers of the Ohio State Radiological Society are: President, Frances A. Miller, M.D., Youngs-

town; President-Elect, Francis C. Curtzwiler, M.D., Toledo; Secretary, Paul D. Meyer, M.D., 125 S. Grant Ave., Columbus; Treasurer, James G. Tye, M.D., Dayton.

The State Radiological Convention will be held in Toledo, May 20-22, 1960.

### WESTCHESTER RADIOLOGICAL SOCIETY

The Westchester (New York) Radiological Society has chosen as officers for the coming year: President, Charles G. Huntington, M.D., White Plains; Vice-President, Clifford C. Baker, M.D., Scarsdale; Secretary, James C. Monteith, M.D., 170 Maple Ave., White Plains, N. Y.

### JAMES PICKER FOUNDATION AWARDS IN RADIOLOGICAL RESEARCH

On behalf of the James Picker Foundation, the National Academy of Sciences—National Research Council announces the award of eight Research Grants, three Grants for Scholars in Radiological Research, and five Fellowships for 1959-1960.

*Grants in Radiological Research:* Dr. Julian L. Ambrus, Roswell Park Memorial Institute, Buffalo, N. Y., for the development of methods to detect areas of myeloid metaplasia; Dr. W. Peter Cockshott, University College Hospital, Ibadan, Nigeria, for the initiation of a program of radiological research; Dr. David W. Cugell, Northwestern University School of Medicine, for an investigation of bronchial dynamics in health and disease; Dr. Bertil Jacobson, Karolinska Institutet, Stockholm, for a quantitative *in vivo* analysis of nonradioactive iodine of the thyroid; Drs. Gwilym S. Lodwick and Theodore E. Keats, University of Missouri Medical Center, for a study of the vascular and osseous changes occurring in hypertrophic pulmonary osteoarthropathy; Drs. Edward B. D. Neuhauser and Abraham M. Rudolph, Children's Medical Center, Harvard Medical School, for continued study of the radiological features of the pulmonary vascular system; Dr. Robert Shapiro, Hospital of St. Raphael, New Haven, Conn., for an investigation of renal venography and inferior vena cavography; Dr. Carl Wegelius, University of Turku, Finland, for research on the use of the narrow beam of x-rays in tomographic methods.

*Scholar Grants in Radiological Research:* Dr. Hugh H. Hayes, Jr., for correlative studies of the roentgenologic and gross anatomy of the central nervous system, at The Johns Hopkins School of Medicine; Dr. Nels M. Strandjord, for research on the x-ray diagnosis of gastric cancer, at the University of Chicago School of Medicine; Dr. Joseph E. Whitley, for radiographic studies of positive intrapulmonary

pressure and of heart defects, and for research on the diagnosis of pancreatic and brain tumors by radio-isotopic means, at Bowman Gray School of Medicine.

*Fellowships in Radiological Research:* Dr. James A. Belli, for study of the influence of temperature upon the biological effectiveness of various qualities of ionizing radiation, at the Southwestern Medical School of the University of Texas; Dr. Ahmad Hatam, for a study of the functional dynamics of the normal physiological activity and pathologic variations of the lower urinary tract, at the University of Louisville School of Medicine; Dr. Gaston R. Vantrappen, for the application of fluorocinematography to the study of gastrointestinal and biliary tract physiology and pathophysiology, at the University of Louvain Medical School, Louvain, Belgium; Dr. Jose A. Veiga-Pires, for a basic radiological investigation using postmortem material, at the Royal Northern Hospital, Holloway, London, England; Dr. Edward C. Wilson, for a critical analysis of gastrointestinal motility, using the technic of cinefluorography and a telemetering capsule, at the University of Virginia Hospital.

## Books Received

Books received are acknowledged under this heading, and such notice may be regarded as recognition of the courtesy of the sender. Reviews will be published in the interest of our readers and as space permits.

### ATLAS OF ROENTGENOGRAPHIC MEASUREMENT.

By LEE B. LUSTED, M.D., Associate Professor of Radiology, University of Rochester School of Medicine and Dentistry, and THEODORE E. KEATS, M.D., Professor of Radiology, University of Missouri School of Medicine. A volume of 176 pages, with 119 figures. Published by The Year Book Publishers, Inc., Chicago, Ill., 1959. Price \$9.00.

### DIAGNOSIS OF CONGENITAL HEART DISEASE:

A CLINICAL AND TECHNICAL STUDY BY THE CARDIOLOGIC TEAM OF THE PEDIATRIC CLINIC, KAROLINSKA SJUKHuset, STOCKHOLM. By SVEN R. KJELLBERG, EDGAR MANNHEIMER, ULF RUDHE, and BENGT JONSSON. A volume of 866 pages, with 727 figures. Published by The Year Book Publishers, Inc., Chicago, Ill., 2d ed., 1959. Price \$28.00.

### BASIC PHYSICS IN RADIOLOGY.

By L. A. W. KEMP, B.Sc., Ph.D., F.Inst.P., Chief Physicist to the London Hospital, and R. OLIVER, M.Sc., F.Inst.P., A.M.I.E.E., Principal Physicist in the Department of Radiotherapy of the United Oxford Hospitals, Oxford, England. A volume of 330 pages, with 143 figures. Published by Charles C Thomas, Springfield, Ill., 1959. Price \$8.50.

**DIAGNOSTIC ROENTGENOLOGY.** ROSS GOLDEN, M.D., editor, Visiting Professor of Radiology, University of California at Los Angeles; Emeritus Professor of Radiology, College of Physicians and Surgeons, Columbia University; formerly Director of the Radiological Service, Presbyterian Hospital, New York. [Renewal pages for Vols. I-III, including: The Roentgen-Ray Examination of the Paranasal Sinuses and the Mastoids, by G. W. Grier, M.D.; Roentgenologic Diagnosis of Diseases of the Urinary Tract, by Marcy L. Sussman, M.D., and George Jacobson, M.D.; The Roentgen Diagnosis of Fractures and Dislocations, by L. Henry Garland, M.B.; Dental Roentgenology, by E. V. Zegarelli, D.D.S.: New Index Pages.] Loose-leaf renewal pages 2.1-2.49; 8.1-8.167; 11.1-11.32; 12.1-12.82; 1169-1210. Published by Williams & Wilkins Co., Baltimore 2, Md., 1959. Price \$60.00.

**THE YEAR BOOK OF CANCER (1958-1959 YEAR BOOK SERIES).** Compiled and edited by RANDOLPH LEE CLARK, JR., B.S., M.D., M.Sc. (Surgery), D.Sc. (Hon.), Houston, Texas, Director and Surgeon-in-Chief, The University of Texas M. D. Anderson Hospital and Tumor Institute; Professor of Surgery, The University of Texas Postgraduate School of Medicine; Clinical Professor of Surgery, Baylor University College of Medicine; Chairman, Committee on Cancer, American College of Surgeons; F.A.C.S., and RUSSELL W. CUMLEY, B.A., M.A., Ph.D., Houston, Texas, Director of Publications, The University of Texas M. D. Anderson Hospital and Tumor Institute; Professor of Medical Journalism, The University of Texas Postgraduate School of Medicine; Executive Editor, Medical Arts Publishing Foundation. A volume of 570 pages, with 202 figures. Published by The Year Book Publishers, Inc., Chicago 11, Ill., 1959. Price \$8.00.

**THE ACUTE RADIATION SYNDROME: A MEDICAL REPORT ON THE Y-12 ACCIDENT JUNE 16, 1958.** Compiled by MARSHALL BRUCER, M.D. From the Medical Division, Oak Ridge Institute of Nuclear Studies, Oak Ridge, Tenn., under contract with the United States Atomic Energy Commission. ORINS-25. A monograph of 188 pages, with numerous figures and tables. Available from Office of Technical Services, Department of Commerce, Washington, D. C., 1959. Price \$1.00.

### THYROID RADIOIODINE UPTAKE MEASUREMENT:

A STANDARD SYSTEM FOR UNIVERSAL INTERCALIBRATION. By MARSHALL BRUCER, M.D., Chairman, The Medical Division, Oak Ridge Institute of Nuclear Studies, Oak Ridge, Tenn. (Under contract with the United States Atomic Energy

Commission.) **ORINS**—19. A monograph of 324 pages, with numerous figures and tables. Available from Office of Technical Services, Department of Commerce, Washington 25, D. C., 1959. Price \$3.50.

**THE COLLECTED STATISTICS OF MALIGNANT DISEASE SEEN AT UNIVERSITY COLLEGE HOSPITAL, LONDON, DURING THE PERIOD 1946-1950.** Compiled by the CANCER FOLLOW-UP DEPARTMENT, University College Hospital, London. A volume of 632 pages. Published by Wilding & Son Ltd., Castle St., Shrewsbury, England, 1958. Price £5.

**COUTES HORIZONTALES DU TRONC: ATLAS ANATOMIQUE ET RADIOLOGIQUE A L'USAGE DES CHIRURGIENS ET DES RADIOLOGISTES.** By RAYMOND ROY-CAMILLE, Prosecteur à la Faculté de Médecine de Paris. Preface by Prof. Gaston Cordier. A volume of 122 pages, with 54 roentgenograms and 54 diagrams. Published by Masson & Cie, 120 Boulevard Saint-Germain, Paris VI, France, 1959. Price 8,000 fr.

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## Book Reviews

LEITFADEN DES STRAHLENSCHUTZES FÜR NATURWISSENSCHAFTLER, TECHNIKER UND MEDIZINER. By Dr. med. HANS R. BECK, Facharzt für Radiologie, Lehrbeauftragter für Strahlenschutz am Badischen Staatstechnikum, Karlsruhe; Dr. rer. nat. HANS DRESEL, Diplomphysiker, Radiologisches Institut der Universität Freiburg/Br.; and Dr. med. HANS-JOACHIM MELCHING, Facharzt für Radiologie, Radiologisches Institut der Universität Freiburg/Br. With a Foreword by Prof. Dr. H. Langendorff, Freiburg/Br. A volume of 254 pages, with 100 figures and 18 tables. Published by Georg Thieme, Herdweg 63, (14a) Stuttgart, Germany, 1959. Distributed in U. S. A. and Canada by Intercontinental Medical Book Corporation, New York 16, N. Y. Price DM 36.—(\$8.60).

The audience for which this guide book on radiation protection is intended, as indicated by the title, includes scientists, technicians, and physicians. The authors have attempted the difficult tasks of condensing a vast amount of material into a relatively small space, and of presenting material for groups of individuals with quite diverse backgrounds. The book covers a wide gamut of subjects relating to radiation protection and includes rather extensive information in the following broad fields: the history of radiation protection; legislation in Germany relating to radiation and its effects; the basic properties of electromagnetic and particulate radiations; nuclear and atomic physics; the detection and measurement of radiations; cosmic radiations; the effects of radiation at the biochemical, cytological, and mammalian levels; early and late effects of radiations on human beings; genetic effects of radiations; the conditions under which man may be exposed to radiation; problems of diagnosis and therapy; the problems of setting up and operating an isotope laboratory; procedural and technical considerations relating to a radiation protection program; and problems of nuclear warfare and civil defense.

On the credit side, it can be said that the authors' material is well organized, the text is well written, and the treatments of the various subjects in general are basic and succinct. An extraordinary wealth of material, with extensive and valuable tables of data, is included, and adequate references for further information are provided. The chapters are so prepared that there is little interdependence, and thus any one can be read separately if desired. Most of the material is up to date, with certain exceptions to be noted below. The authors have endeavored to provide information of practical

value and sometimes procedures, not commonly covered in books of this nature, are outlined, as, for example, practical methods of wound decontamination. A glossary is provided which is adequate as far as it goes. It is limited, however, mainly to medical terms, and one wonders why more physical definitions were not included for the benefit of the individual with a background in the biological sciences and relatively little in the physical sciences. The book has the virtue of an index.

On the debit side, the efforts to compress data and to reach an audience of varied background has of necessity led to shortcomings. In the attempt to embrace too much material, adequacy of coverage and clarity have frequently been sacrificed for brevity. For the expert, the text is not necessary and the material covered is not sufficiently extensive to provide an adequate reference work. For the nonexpert, the treatment of most subjects is too brief and too technical. Thus the book would not be particularly suited for self-teaching unless one were already fairly well grounded in both the biological and physical sciences. Frequently superfluous material is included. For instance, the spin of nuclear particles is included in tables without further explanation of meaning or use. The balance of emphasis can also be questioned. For example, considerable space is devoted to the theory and construction of the betatron; on the other hand, the treatment of the important subject for radiation protection, the interactions of ionizing corpuscular radiations with matter, is too short and too technical for those to whom the book is addressed. The work would be markedly improved if more space could be allotted to each of the subjects covered.

Some of the radiobiology included is misleading, some out-dated, and some at variance with the views and experiences of the reviewers. The statement is made that anemia is a very serious consideration in radiation injury, which it is not in the absence of hemorrhage. Values given for RBE factors are conservative and not consistent with current data. The concept of a circulating heparin-like substance being responsible for radiation-induced hemorrhage is retained and protamine and toluidine blue are recommended in treatment, a concept abandoned some years ago. The authors leave the distinct impression that human bone-marrow transplants "take," and the procedure is recommended for the treatment of radiation injury. "Takes" of such transplants in human beings remain to be demonstrated conclusively and many factors must be taken into account when the problem of bone-marrow transplantation arises. Some lack of critical evaluation of data and concepts is in evidence. For instance, the authors apparently feel that irradiation of the midbrain may be efficacious in the treatment of radiation ulcers. The chapter on genetics does not give a sufficiently complete picture of the consequences involved in the "doubling dose" concept.

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Despite the above-noted difficulties, the reader in the intended audience will find the book concise and informative, and the wealth of information will be of considerable value. He will be able to find a treatment of most of the myriad subjects connected with radiation safety, and, in conjunction with the references, should be able to satisfy his needs in this field. The work represents a compromise between a short handbook of data alone and the extensive volumes on this subject available.

## In Memoriam

HERBERT A. MAHRER, M.D.  
1892-1959

Dr. Herbert A. Mahrer, a long-time member of the Radiological Society of North America, died on July 16, 1959, in the Mount Sinai Hospital of Cleveland, the day following a coronary artery occlusion.

A life-long resident of Cleveland, Dr. Mahrer was graduated from Adelbert College and the Medical School of Western Reserve University, receiving his medical degree in 1917. He served his internship and residency at Mount Sinai Hospital and began the private practice of internal medicine with Dr. A. S. Maschke. After two years he became interested in radiology and, following a short period of study here, went to Vienna, where he spent a year under the tutelage of the then acknowledged leaders of that specialty.

On his return to Cleveland in 1923, Dr. Mahrer became associated with Dr. Edward Freedman, then Chief of Radiology at Mount Sinai, both at the hospital and in the office practice of radiology. Following Dr. Freedman's death in 1947, younger men entered into the association, so that at Dr. Mahrer's death he was the senior partner in a seven-man group. He became Chief of the Department of Radiology at Mount Sinai Hospital in 1947 and served with distinction until his retirement from that position on June 30, 1958. He had been President of its Medical Council for two years. He was a past president of the Cleveland Radiological Society. Following his first coronary occlusion several years ago, he had gradually lightened his work load and had become a winter time resident of Sarasota, Florida.

Dr. Mahrer made a lasting contribution to the practice of radiology in Cleveland. A firm believer in the virtues of combining the independence of practice with the intellectual stimulation of a teaching hospital department, he successfully pursued this policy and has left a firm foundation for his associates to follow. His opinions were

universally respected, as was his intellectual honesty. No contributor to the literature, he read widely and applied clinical principles to the practice of radiology. He was known as a keen observer whose eye missed nothing on the film.

While Dr. Mahrer was always a generous giver to worthy charities, his never ending private giving to those in need was known to only a few of his intimates.

Although he was slightly handicapped by polio as a boy, he always maintained an interest in sports and until his later years was an active bowler. An avid bridge player, he was recognized as an expert and participated in local tournaments.

His wise and calm counsel will be missed by his lay and professional friends alike. He is survived by his wife, Florence Lossing Mahrer.

GEORGE R. KRAUSE, M.D.

PATRICK F. BUTLER, M.D.  
1877-1959

Dr. Patrick F. Butler—"Paul," as he was known to most of his confreres—died on June 29, 1959, at the age of eighty-two. His premedical studies were pursued at Holy Cross College, Worcester, Mass., and at Harvard College, following which he entered Harvard Medical School being graduated in 1903.

He served an internship of eighteen months in surgery at the Carney Hospital and later spent some years in general practice. He then took up roentgenology, as it was known in those days, and became chief of that department at the Carney Hospital. In 1922, he went to the Boston City Hospital, where he became Director of the Department of Radiology and remained until his resignation in 1945. Passing through the grades from Instructor to Clinical Professor of Radiology at Harvard Medical School, he had the opportunity of teaching, which he enjoyed, and training many of our younger radiologists who are in responsible positions throughout the United States and Latin America.

Dr. Butler was a member of the Radiological Society of North America, the American Roentgen Ray Society, of which he was president in 1926, the American College of Radiology, the American Medical Association, and the New England Roentgen Ray Society, which he served as president in 1923-24. Holy Cross College conferred upon him the honorary degree of Doctor of Science in 1957. He delivered the George W. Holmes Lecture of the New England Roentgen Ray Society in 1938.

Always urbane, never given to controversy, Dr. Butler continued in active practice until a few months before his death from pancreatic disease. He was predeceased by his wife and left no children.

FREDERICK W. O'BRIEN, M.D.



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## ROENTGEN DIAGNOSIS

### THE HEAD AND NECK

**Cerebral Angiography: A New Technique.** Catheterization of the Common Carotid Artery via the Superficial Temporal Artery. Israel H. Weiner, Nicholas M. Azzato, and Robert A. Mendelsohn. *J. Neurosurg.* 15: 618-626, November 1958. (Lackland Air Force Base Hospital, Texas)

A new technic of cerebral angiography is described which utilizes catheterization of the carotid system via the superficial temporal artery. The incision is made in the preauricular region over the palpable temporal artery. The plastic catheter used was the Clay-Adams Intramedic No. PE 190/S12, which is supplied in individual sterile packages in 30-cm. lengths. The catheter is advanced 12 to 15 cm. inferiorly in the artery, which places the end in the common carotid.

Sixty-five successful angiograms in 48 persons were obtained with this technic. On 4 occasions, early in the study, the acute turn of the artery around the zygoma obstructed passage of the catheter. By exposing the artery low in the region of the turn and directing the catheter inward when that point was reached, this problem was eliminated. Adequate filling of the carotid system was uniformly obtained, in spite of retrograde injection.

There were no complications due to ligation of the temporal artery. In 6 cases, including 3 with bilateral ligation, there was uneventful healing of the scalp flaps. Only one major complication occurred, and this is attributed not so much to the particular technic employed as to angiography in general or possibly to the progression of a prior disease process. A forty-year old male had had a two-hour episode of left hemiplegia. It recurred two months later, twenty-three hours after a right carotid arteriogram.

Jaeger and Whiteley reported an intravascular intubation technic for cerebral angiography in 1955 (*Am. J. Roentgenol.* 73: 735, 1955. *Abst. in Radiology* 66: 454, 1956) and claimed for it the following advantages, which hold equally for the procedure described here: (1) elimination of the danger of extravascular injection, thus making Thorotrast a more desirable medium, (2) prevention of mechanical damage to the artery, (3) precise injection of the internal carotid artery, (4) elimination of the strain of maintaining a sharp needle immobile in the artery, (5) freedom for proper positioning, and (6) allowance for leisurely, accurate study. Because of the freedom of movement, postero-anterior, optic canal and other oblique views have been employed, when indicated, with improved definition and detail of the vasculature. A seventh advantage is the visualization of the external carotid system, which may be desirable in certain cases of neoplasms, vascular malformations, and occlusions.

Disadvantages of the technic are its relative complexity and the time required, the possibility of wound infection, the small scar, the sacrifice of the artery, and the routine filling of the external carotid system.

Other possible applications of the method mentioned by the authors include retrograde vertebral angiography, cerebral angiography in children, subclavian angiography, and aortography.

Three roentgenograms; 1 drawing.

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**Cerebral Angiography: Clinical Experience with Comparative Contrast Media.** Ralph A. Munslow, Francis E. O'Neill, Richard D. Price, Alvin Thaggard, Jr., Robert C. Hardy, and Jerome J. Wiesner. *Texas State J. Med.* 54: 725-728, October 1958. (414 Navarro St., San Antonio 5, Texas)

In a study of the cerebral angiograms in 250 cases, the authors attempted a comparative evaluation of Diodrast in 35 per cent solution, Hypaque 50 per cent, and Renografin 60 per cent.

The angiograms obtained with Renografin or Hypaque were superior to those made with Diodrast.

One death and 3 instances of hemiparesis and/or aphasia of a permanent nature were found in 100 cases in which Diodrast was the agent. No permanent neurologic sequelae and only 4 cases of transient paresis followed angiographic study in 150 cases where Hypaque or Renografin was the medium employed. In at least 2 of these 4 cases a small air embolus in the injection system rather than the radiographic material was responsible. Whereas transient erythema was consistently noted within the domain of the external carotid circulation on the side of injection when Diodrast was the agent used, there was little or no similar reaction following Hypaque or Renografin administration. If inadvertently injected outside the lumen of the carotid, Hypaque and Renografin seemed to cause no local reaction and little pain.

Seven roentgenograms.

**The Relationship Between Findings in Pneumoencephalograms and Clinical Behavior.** Hilda Knobloch, Martin P. Sayers, and William H. R. Howard. *Pediatrics* 22: 13-19, July 1958. (561 S. 17th St., Columbus 5, Ohio)

In order to determine what correlation exists between pneumoencephalographic and clinical behavioral findings, three independent evaluations were done with 50 patients. A radiologist and neurosurgeon each classified the roentgenograms according to the presence or absence of ventricular dilatation, abnormality of cortical marking, and other abnormalities. A pediatrician did Gesell developmental examinations and made estimates of intellectual potential and neurologic status. There was no significant correlation of adaptive and gross motor developmental quotients with the pneumoencephalographic diagnoses. Neither was a statistically significant correlation obtained between the pneumoencephalographic findings and the presence or absence of mental retardation or certain neurologic abnormalities. Age at examination did not vary significantly with the clinical diagnosis, but the mean age of patients with abnormal air studies was less than one year compared to approximately two and a half years for those with normal pneumoencephalograms. It was concluded that it is not feasible to predict intellectual functioning on the basis of pneumoencephalographic findings alone, particularly in children less than one year of age.

Two charts; 5 tables.

**Subarachnoid Hemorrhage. Prognosis When Angiography Reveals No Aneurysm. A Report of 138 Cases.** Olle Höök. *Acta med. scandinav.* 162: 493-503, 1958. (Serafimerlasarettet, Stockholm, Sweden)

During the period from 1934 to 1955, 138 cases of



spontaneous subarachnoid hemorrhage in which angiography failed to reveal arterial aneurysms or other sources of bleeding were treated in the neurologic and neurosurgical clinics of Serafimerlasarettet (Stockholm). The average age of the patients at the time of admission to the hospital was forty-three years; men and women were equally represented. These cases have been followed for an average of four and a half years. Only 2 of the 139 patients could not be traced. Two patients died within eight weeks of the hemorrhage and 14 died after two months or more; 6 in the latter group died from other diseases.

Patients were placed in six different risk groups according to their clinical condition, following a classification system employed in an earlier investigation:

Group A<sub>1</sub> (1 patient): Patients who were in deep coma on admission, usually with Cheyne-Stokes breathing and other signs of failing vital centers. The majority of these patients were considered moribund or nearly moribund.

Group A<sub>2</sub> (6 patients): Patients who were in a semi-conscious state on admission, usually disoriented as to time, place, and identity, and usually with severe neurologic signs.

Group B<sub>1</sub> (6 patients): Patients seen within two weeks after their last hemorrhage, initially in coma but partially completely recovered from comatose state at the time of admission.

Group B<sub>2</sub> (16 patients): Patients seen within two weeks after their last hemorrhage without initial coma and partially or completely recovered at the time of admission.

Group C (33 patients): Patients seen more than two weeks but within eight weeks after their last hemorrhage, who had recovered partially or completely at the time of admission.

Group D (76 patients): Patients seen eight weeks or more after their last hemorrhage.

Nine patients had severe focal signs, 38 slight focal signs usually of transient character, and 91 no focal signs. One patient was seen with subarachnoid hemorrhage without focal signs in 1951. Bilateral carotid and vertebral angiography showed no abnormality. In 1953 the patient had another subarachnoid hemorrhage and at that time a large ependymoma was demonstrated. Coarctation of the aorta was found in another case. The late prognosis with respect to recurrent fatal hemorrhage was favorable, with an incidence of 6 per cent. Eighty per cent of the patients had only one hemorrhage, 15 per cent had 2 hemorrhages, and 5 per cent 3.

Bilateral carotid angiography was performed in 86 patients, bilateral carotid and vertebral angiography in 48, and unilateral carotid and vertebral angiography in 4. In the large majority of cases angiography was not done until at least three weeks after the subarachnoid hemorrhage. In 2 cases in which bilateral carotid angiography was done with negative results, arterial aneurysms were disclosed at autopsy. The author reviewed the films in 60 of the 86 cases in which bilateral carotid angiography was performed. In 15 cases the posterior cerebral artery was filled on both sides; in 25 on neither [text reads either, which appears to be an error] side. In 20 cases one side was filled; the proportion of right to left was 2:1.

A definitive answer to the question of the different causes and their relative incidence in cases of subarachnoid hemorrhage in which angiography does not reveal

the presence of aneurysm is impossible without access to a more extensive autopsy material that has been subjected to thorough neuropathologic study.

The indications for vertebral angiography are briefly discussed. The author believes it should be performed when bilateral carotid angiography fails to show any source of the bleeding (1) if there are neurologic symptoms from the vertebral-basilar region; (2) in young patients; and (3) in recurrent hemorrhages. In the future the indications for this examination will probably be further broadened.

Treatment was conservative in all cases. At the time of follow-up, 80 of the 120 surviving patients who could be traced were symptom-free and able to work; 27 had slight residual symptoms, which usually reduced their capacity to work very little or not at all; and 13 considered themselves completely unable to work. In the last group, the reduced working capacity in 3 or perhaps 4 cases was not due to the sequelae of the subarachnoid hemorrhage.

Three roentgenograms; 2 charts; 7 tables.

**The Sella in Health and Disease. The Value of the Radiographic Study of the Sella Turcica in the Morbid Anatomical and Topographic Diagnosis of Intracranial Tumours.** Mahmoud El Sayed Mahmoud. Brit. J. Radiol. Suppl. No. 8, 1958. (Cairo University, Cairo, Egypt)

The author studied in detail 617 cases of confirmed intracranial masses and 2,000 skulls without intracranial lesions. The intracranial tumors have been considered in relation to the changes produced in the sella, and the author's observations are painstakingly compared with those of others as reported in the literature.

The tumors are classified as follows: tumors of the sellar walls; intrasellar tumors; perisellar tumors (presellar, suprasellar, parasellar, retrosellar); metasellar tumors, this last group comprising the more remote intracranial tumors.

In metastases of the *sellar walls* no sellar changes are detectable radiologically. Malignant tumors invading from below tend to destroy the floor and dorsum.

The cardinal changes in cases of *intrasellar tumors* are: enlargement of the sella, with expansion of its floor, which is frequently irregular; retention of the posterior clinoid processes; destruction of the dorsum sellae, more marked at its base. It is the author's opinion that retention of the posterior clinoids and destruction of the dorsum advancing from the base are pathognomonic of an intrasellar mass even without marked sellar enlargement.

Sellar changes were observed in 34 of the 63 *perisellar tumors* studied. Presellar tumors produced no characteristic changes; parasellar tumors caused unilateral changes; retrosellar masses tended to destroy the dorsum sellae. The picture in suprasellar tumors is not constant. The cardinal sellar changes in this group are a widening of the outlet in the anteroposterior diameter without increase in depth, resulting in a shallow sella, and erosion of the posterior clinoid processes and the tip of the dorsum sellae. The sellar floor is unusually regular.

Diminished density or bone discontinuity of the sellar walls usually accompanied *metasellar tumors*, but was without localizing value. The author discusses at some length the mechanism of sellar change in this group of tumors. He believes that, with generalized increase of intracranial tension due to a growing tumor, the pres-

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sure is transmitted equally to the whole of the inner surface of the skull, but the dorsum sellae and posterior clinoid processes show the effect first.

A moth-eaten appearance of the sellar walls was found to be due to infiltration by meningioma.

The close association of the sphenoid sinus with the floor of the sella turcica plays an important part in retarding pathological changes in the latter in the presence of intracranial tumors. The cortical wall of the sinus, when adjacent to the cortical floor of the sella, offers a formidable barrier to forces which would normally cause sellar enlargement.

One hundred twenty figures; 9 tables.

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**A Technic for Arteriography of the External Carotid Artery.** Giovanni Ruggiero and Maurice Jay. *Acta radiol.* 50: 453-459, November 1958. (In French) (Hôpital Sainte-Anne, Paris, France)

The main indications for arteriography of the external carotid artery are: (1) demonstration of involvement of the vessels of the dura mater in an intracranial arteriovenous aneurysm, (2) study of extracranial tumors and vascular malformations with or without intracranial extension, (3) definition of contours of a meningioma, and, most important, (4) differentiation between a meningioma and an intracerebral vascular tumor.

Hazards of transcutaneous puncture of the external carotid are mainly puncture of either the common or the internal carotid artery. This is obviated by having the patient lie on his back with neck deflected and head turned toward the opposite side. In this position the cornu of the hyoid bone is easily found, and a line may be drawn from this point to the angle of the mandible. The puncture is made in this line, some millimeters above the hyoid. The authors have done a total of 56 examinations with 3 failures.

While the degree of extension and rotation of the neck varies according to the subject, the optimal position is indicated by the pulsation of the artery.

The technical points are elaborated upon.

Two roentgenograms; 2 photographs; 2 diagrams.

CHRISTIAN V. CIMMINO, M.D.  
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**Ipsilateral Carotid Thrombosis in Hemiparesis.** E. Stricker and M. Klingler. *Schweiz. med. Wchnschr.* 88: 1191-1193, Nov. 22, 1958. (In German) (Medizinische Universitätsklinik, Basel, Switzerland)

Eight cases of hemiparesis are reported in which angiography revealed ipsilateral occlusion of the internal carotid artery. In 4 of these patients, an additional obstruction of major vessels was found to be responsible for the symptoms. In the remainder the carotid occlusion was the only demonstrable abnormality. The significance and pathogenic meaning of this finding are discussed in connection with a case of post-traumatic hemiplegia, which was erroneously attributed to traumatic carotid occlusion.

Three roentgenograms.

**Observations on Congenital Anomalies in Teeth and Skull in Two Groups of Mental Defectives (Comparative Study).** Richard Spitzer and R. L. Quilliam. *Brit. J. Radiol.* 31: 596-604, November 1958. (The Fountain Hospital, London, S.W.17, England)

A comparative study of the radiographic and clinical

findings in the cranial and facial bones of mentally defective children is presented. The material consisted of a group of 20 mongolian idiots, 18 microcephalics, and 2 undifferentiated defectives. All the patients showed developmental lesions of congenital origin.

The characteristic findings in the mongoloid series were:

1. Disproportion between the size and development of the cranium as compared with facial bones; maxillary and mandibular micrognathia associated with retarded growth of other parts of the facial skeleton.

2. Failure of development of frontal sinuses. In none of the 20 cases were the frontal sinuses demonstrable radiographically.

3. Dental anomalies, including defects of shape, size, structure, time of eruption, and agenesis of individual teeth, present in all 20 cases.

4. Persistence of the metopic suture in 15 patients (5 after the age of ten).

In the microcephalic group there were found:

1. Underdevelopment of the cranial vault, with abnormal contour of the forehead and occiput, and hypoplasia of the anterior cranial compartment.

2. Normal development of the facial skeleton.

3. Good pneumatization of frontal sinuses, with 4 exceptions.

4. Normal closure of the metopic suture.

5. No dental anomalies.

The radiographic findings in these two groups of mental defectives are distinctive. Particular attention should be paid to development of the cranial vault, facial growth, dental anomalies, paranasal sinuses, and the status of the metopic suture.

Twelve roentgenograms; 2 tables.

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Lackland AFB, Texas

**Congenital Anomalies of the Sound-Conducting Organs.** Pekka Soila. *Acta radiol.* 50: 444-452, November 1958. (University of Helsinki, Finland)

Congenital anomalies of the sound-conducting organs are described. These are of rare occurrence, but the author reviews the radiographic and surgical findings in 74 cases, with bilateral involvement in 10. Division into four grades roentgenologically according to the condition of the ossicles and the tympanic cavity is suggested. In Grade I the tympanic cavity is of about normal size and sharply demarcated, containing air; the head of the malleus, the body of the incus, and the joint are discernible. In Grade II the form, air content, and margins of the tympanic cavity vary, but the head of the malleus can be seen. In Grade III the ossicles form a conglomerate mass in a deformed tympanic cavity and the malleolar head is not demonstrable. Grade IV consists in complete obstruction of the tympanic cavity and absence of a cellular system.

Two of the 84 ears which were examined were not operated upon; in 3 only a minor correction was done, and in 9 cases the findings at operation were not in accord with the roentgen observations. In 7 out of every 8 cases it was possible to determine the details of congenital malformations roentgenographically. Errors were due to failure to demonstrate the tympanic cavity.

The submentovertical projection and lateral stereoscopic views with the tube tilted 30° cranially were used routinely. In 2 cases in which the roentgen and surgical findings were in disagreement it was felt that planigrams would have been useful.

Prominent in this group of abnormalities is hypoplasia or absence of the external auditory canal. Malformations of the condyloid process and the temporomandibular fossa may also be evaluated and are found to increase with the degree of middle-ear anomaly.

Seventeen roentgenograms; 2 tables.

MAJ. NEIL E. CROW, M.C.  
Lackland AFB, Texas

### THE CHEST

**Clinical, Radiographic, and Pathological Studies of the Lungs of Electric-Arc and Oxyacetylene Welders.** H. E. Harding, A. I. G. McLaughlin, and A. T. Doig. *Lancet* 2: 394-398, Aug. 23, 1958. (A.T.D., Lecturer on Industrial Hygiene, University of Aberdeen, Scotland)

It is generally believed that the inhalation of iron-oxide dust does not lead to fibrosis in the lungs or produce disability, but that the retained dust produces x-ray shadows that may be indistinguishable from fibrotic pneumoconiosis. The condition is usually called "siderosis." Welders and oxyacetylene cutters commonly inhale iron-oxide fumes, and not infrequently there are shadows in the roentgenograms of their lungs. Few welders, however, are exposed only to iron oxide: some of them work in places such as the fettling shop, where there is a mixed silica dust produced by other operations; most of them use rods coated with various materials; the metal which they work on may not be iron or may contain metals other than iron; if they work in enclosed spaces, oxides of nitrogen and possibly other gases may irritate the respiratory tract.

Details are given of 4 electric-arc welders and 1 oxyacetylene cutter who came to necropsy. So far as could be ascertained, none of the welders had been exposed to any obvious risk from silica dust, but all had used coated electrodes and 1 had been exposed to fumes from burning paint. Two cases showed very slight mixed-dust fibrosis with nodules that were just visible and palpable after twenty-nine and twenty-eight years welding; another showed mixed-dust fibrosis of insignificant degree, discovered microscopically after more than thirty years. The fourth welder had no fibrosis after forty years welding. In none was the mixed-dust fibrosis held responsible for death or for any recognizable disability.

The oxyacetylene cutter had a slight accumulation of dust in his lungs and no fibrosis, but he had worked as a cutter for only nine years, with a twelve-year break between two periods of cutting.

The authors consider that it is established beyond doubt that considerable quantities of pure iron oxide can be inhaled and remain deposited in the lung tissue without producing fibrosis. Slight degrees of fibrosis may be present in the lungs of some electric-arc welders, but this is believed to be caused not by iron oxide but by other constituents of the welding fume, or possibly by some of the gases evolved. The degree of fibrosis present, even in welders with long experience, has not been sufficient to cause any disability. More severe degrees of fibrosis amounting to mixed-dust pneumoconiosis, associated in some cases with disability, have, from the authors' observations, occurred only in welders exposed to extraneous sources of silica, such as that found in fettling shops of foundries.

Two roentgenograms; 6 photomicrographs; 1 photograph.

**Local Reactivation of the Primary Tuberculous Focus in the Lung.** J. Snijder and Th. Vossenaar. *Am. Rev. Tuberc.* 78: 547-562, October 1958. (Sanatorium "Berg en Bosch," Bilthoven, Netherlands)

The authors studied reactivation of the primary tuberculous complex in patients in whom it had been inactive for a long time, often for a number of years. Among a total of 4,554 tuberculous patients, they found 12 suffering from such local reactivation. Seven of these patients were fourteen years and under, 3 of the remainder were in their teens, 1 was twenty-four, and 1 was twenty-seven years of age, indicative of a definite predilection for young patients. In the 8 patients in whom the interval between the detection of an active primary complex and its reactivation could be established, it averaged approximately three and one quarter years. This coincides with the impression that local reactivations usually develop within the first few years after subsidence of the primary complex. Several examples are given, with radiographic and photomicrographic illustrations to show the course of the disease radiographically and the morphology when resection was carried out.

Liquefying caseous foci were present, usually around an old calcified focus or adjacent to one edge of it. Viable tubercle bacilli were found in the recent focus. Some of the small excavations could be demonstrated by tomography, while others showed only an enlargement of the nodule in a rather eccentric manner.

The authors regard local reactivation as an indication for pulmonary resection because of the liquefaction and the tendency to periodic progression.

Six roentgenograms; 10 photomicrographs; 2 photographs.

JOHN H. JUHL, M.D.  
University of Wisconsin

**Diffuse Interstitial Pulmonary Fibrosis (Hamman-Rich Syndrome). Report of Three Cases.** Robert J. Carabasi. *Am. Rev. Tuberc.* 78: 610-622, October 1958. (Scott and White Clinic, Temple, Texas)

The condition described by Hamman and Rich in 1944 (*Bull. Johns Hopkins Hosp.* 74: 177, 1944. *Abst. in Radiology* 43: 405, 1944), and since known by their names, is characterized by progressive, diffuse fibrosis of the pulmonary alveolar walls which starts as an acute inflammatory process and progresses to complete fibrosis. The varying stages of the disease can be found in a single specimen indicating increasing involvement of pulmonary tissue.

In the 3 cases reported here autopsy showed varying stages of fibrosis and smooth muscle proliferation without much inflammatory reaction. One of the patients lived fifteen years following the onset of symptoms, representing the longest survival on record. Roentgenograms of 2 of the patients are included, showing a rather diffuse process with changes ranging from slight accentuation of markings in the apices to coarse accentuation in the mid zones and conglomerate densities in the bases. These findings were progressive, but basal changes were more pronounced than the changes elsewhere in the lungs. In 1 of the patients the hili appeared to increase in size, suggesting adenopathy but its presence is not reported in the autopsy. Corticosteroid therapy is discussed and the author believes that this is indicated if the diagnosis is made early.

Five roentgenograms; 5 photomicrographs.

JOHN H. JUHL, M.D.  
University of Wisconsin

**Idiopathic Mediastinal Fibrosis.** N. R. Barrett. *Brit. J. Surg.* 46: 207-218, November 1958. (London, England)

Idiopathic mediastinal fibrosis is a clinical and pathological entity of unknown etiology, characterized by abnormal fibrous proliferation of tissue in the mediastinum. The clinical hallmark is the presence of venous hypertension in the drainage area of the superior vena cava. The hypertension is due to the fibrous tissue that engulfs, invades and destroys some or all of the great veins uniting to form the superior vena cava. The condition is a rare one, affecting both sexes and all age groups.

The clinical picture is usually of sudden onset, and symptoms may be intermittent at the start. The face may swell for a few days or a collar feel tight. Puffiness of face and arms is usually the earliest manifestation. Later the face, neck, and arms assume a dusky color, and other symptoms may appear, as headaches, dizziness, dyspnea, and epistaxis. After several months a gradual improvement sets in, due to establishment of collateral circulation. Laboratory tests and chest films are negative.

Diagnosis of idiopathic mediastinal obstruction is achieved by phlebography of the mediastinal veins. This is performed under general anesthesia, with catheters passed into a vein in each arm. An opaque medium is injected and serial films are made. Such a study usually reveals the vein obstruction and the dilated collateral circulation, mainly from the azygos system.

The cases explored show dense, hard fibrotic tissue involving the vessels of the superior mediastinum. Histologically, this is collagenous tissue, with scattered small-cell infiltration. Cultures show no incriminating organisms. The author suggests a similarity between this condition and idiopathic retroperitoneal fibrosis, pseudotumor of the orbit, and Riedel's disease in the thyroid.

The disease is self-limiting, seldom kills, and is compatible with a long life in which the patient can work, although at some disadvantage. There is no medical treatment. Surgical by-pass or replacement grafts have been occasionally successful, but more often fail due to thrombosis in the graft.

Three roentgenograms; 1 photograph; 3 diagrams.

J. S. ARAJ, M.D.

Toledo, Ohio

**Suspicion of Lung Cancer.** H. Birkhäuser. *Schweiz. med. Wchnschr.* 88: 500-506, May 17, 1958. (In German) (Tuberkulose-Beratungsstelle, Basel, Switzerland)

The simultaneous occurrence of different pulmonary diseases in the same patient is discussed by the author, who reports 17 cases in which a lung tumor was suspected in association with pulmonary tuberculosis or other chronic lung condition.

Whenever unexpected pulmonary densities are encountered in older males who have been treated or observed for many years for an indurative inactive or even active pulmonary tuberculosis without demonstration of tubercle bacilli in the sputum, the possibility of a carcinoma should be considered. Since scar tissue seems to favor malignant change, routine periodic chest films are particularly valuable in these instances.

The tuberculin skin reaction is often helpful, especially when it is rather weak in the presence of an infiltration or coin lesion. In one of the reported cases

this special finding led to an exploratory thoracotomy which resulted in detection of a tumor.

Aid is frequently obtained from microscopic studies of lymph nodes or scalene biopsy material. Bronchoscopy was of little value in the majority of the author's cases. In a few instances, particularly when patients refused surgery, dependence had to be placed on conservative observation instead of the customary exploratory thoracotomy.

Most of the patients in the author's series were males over forty years of age. In this group, a history of recurring bouts of pneumonia involving the same segment, dense infiltrations with delayed resolution, and persistent cough with deterioration of the general condition are suggestive of a neoplasm, especially if the sputum is negative for tubercle bacilli.

Lateral and oblique views of the chest, with fluoroscopy, are recommended in addition to the routine postero-anterior view. Examination of the esophagus with barium paste will help rule out esophageal tumors or extrinsic masses displacing or compressing the esophagus and exerting pressure on the trachea. Negative bronchoscopic, bronchographic, and cytologic findings never rule out a bronchogenic tumor, nor does a normal sedimentation rate.

In most of the author's series of 17 cases pulmonary cancer was found to be present. One patient had a leiomyoma of the esophagus exerting pressure on the right upper bronchus, causing persistent cough without expectoration. Two other cases may be cited to illustrate the diagnostic problem. In each of these there was a ring-like shadow in the lung. In one, absence of lymphovascular linear shadows between the lesion and the hilus suggested a liquefying tumor, and this diagnosis was confirmed on thoracotomy. In the other case the lymphovascular markings led to a diagnosis of isolated tuberculous cavity.

Unfortunately, there is no relationship between the size of a carcinoma and the possibility of metastasis, as very small tumors are often found with general metastasis on the first roentgen examination.

It is recommended that special care be taken when a lung cancer is suspected in a heavy smoker, as there appears to be a definite causal relationship. Thoracotomy should always be performed in those patients in whom the possibility of a tumor cannot be definitely ruled out by other means.

Twenty-nine roentgenograms.

HERBERT POLLACK, M.D.

Chicago, Ill.

**Surgical Experiences with Pulmonary Coin Lesions.**

Otto V. Hibma and Edward I. Boldon. *Wisconsin M. J.* 57: 359-364, October 1958. (16 E. Gorham St., Madison, Wisc.)

A series of 24 coin lesions is reported, 3 of which (12.5 per cent) proved to be cancer. Eighteen (75 per cent) were granulomas, 1 was a neurofibroma, 1 a pleural fibroma, and 1 an infarct (?). While the authors agree in general with those recommending removal of all coin lesions, they make certain specific exceptions. They believe that the presence of multiple, well calcified lesions on the roentgenogram constitutes satisfactory evidence of benignity. Lesions which are solidly calcified throughout also seem to merit observation, as do partially calcified lesions which can be shown roentgenographically to have been stable over a period of at least one year.

## THE HEART AND BLOOD VESSELS

**Ventricular Septal Defect in Infants and Children: A Correlation of Clinical, Physiologic, and Autopsy Data.** Donald C. Fyler, Abraham M. Rudolph, Martin H. Wittenborg, and Alexander S. Nadas. *Circulation* 18: 833-851, November 1958. (Harvard Medical School, Boston, Mass.)

Ninety-eight cases of proved (by catheterization) ventricular septal defect were studied in respect to the natural history of the condition, in the hope of arriving at some working hypothesis in regard to operative indications.

Most of the patients had moderate or marked enlargement of the heart demonstrable by x-ray. It was interesting that some persons with small shunts had large hearts, and rarely those with pulmonary vascular obstruction and large left-to-right shunts had relatively small hearts. Estimation from the films of which ventricle was preponderant proved inaccurate, but the electrocardiogram was reliable in this respect. The presence of an enlarged pulmonary artery seemed to indicate either pulmonary vascular obstruction or a large left-to-right shunt. The left atrium was usually enlarged.

The size of the shunt seemed to undergo a change in some patients, evidenced by a decrease in symptoms and heart size or by deterioration and development of congestive failure. Those with pulmonary vascular obstruction were the most stable group over the period of observation.

Patients with moderate cardiac enlargement and electrocardiographic findings of pure left ventricular hypertrophy were the best candidates for surgery. Children with pure right ventricular hypertrophy, irrespective of heart size, have either associated pulmonary vascular obstruction or pulmonary stenosis. Those with pulmonary stenosis are candidates for surgery, while in those with pulmonary vascular obstruction the risk of operation should probably not be taken. Cases with enlarged hearts and combined ventricular hypertrophy must be considered on an individual basis, depending on the catheterization findings.

Sixteen figures, including 8 roentgenograms; 14 tables.

ZAC F. ENDRESS, M.D.  
Pontiac, Mich.

**Situs Inversus Totalis Associated with Complex Cardiovascular Anomalies.** Karl J. Schmutzer and Leonard M. Linde. *Am. Heart J.* 56: 761-768, November 1958. (University of California Medical Center, Los Angeles, Calif.)

Severe cardiac abnormalities may accompany situs inversus, though their incidence is low (8 per cent). Two cases are presented. The first patient, a five-month-old female, had a cardiac murmur with signs of decompensation. X-ray examination showed a complete situs inversus, a boot-shaped heart, and decreased pulmonary vascularity. Cardiac catheterization revealed pulmonic stenosis, and angiocardiology disclosed an interventricular septal defect and an anomalous pulmonary vein draining into the superior vena cava.

The second patient was a fifteen-year-old girl with signs of cardiac decompensation. She had had pneumonia at the age of nine months and roentgenograms at that time had revealed situs inversus. A ventricular septal defect and absence of the inferior vena cava, with

functional replacement by the azygos vein, were diagnosed.

Recent advances in cardiovascular surgery have made it necessary for clinicians to obtain a more complete understanding of the embryologic development of cardiac anomalies. Knowledge of situs inversus dates back to the time of Aristotle and discussions at that time were concerned mainly with mythical speculation. A later theory suggested that this condition was related to the development of double monsters, and still later it was believed to be due to rotation of the embryo to the right instead of to the left. At the present time it is felt that structural changes within the ovum or the zygote are responsible.

Six roentgenograms; 2 tables.

ROGER M. STOLL, M.D.  
New York, N. Y.

**Functional Diagnosis of Patent Ductus Arteriosus Studied by Cineangiocardiology in Fifty-Three Cases.** Frank L. Campeti, Raymond Gramiak, James S. Watson, and George H. Ramsey. *Circulation* 18: 887-896, November 1958. (University of Rochester School of Medicine and Dentistry, Rochester, N. Y.)

Densitometric analysis of selected areas of cineangiograms was done in 53 cases of patent ductus arteriosus. The pulmonary artery bifurcation and the left branch were the areas studied in various phases of the cardiac cycle. The amount of light transmitted through these vessels depends on the cross-section area as well as on the amount of contrast medium within. In normal subjects there is a decrease in density during diastole because of mixing of the contrast medium with the blood present in the vessel during the first and second cycles. In subsequent cycles the decrease in opacity in diastole is considerably greater in the patient with patent ductus than in the normal subject, because of dilution by the nonopacified blood shunted into the pulmonary artery through the ductus from the aorta. Study of time relationships showed that most of the flow through the ductus appeared to be in diastole.

The presence of other complicating anomalies did not interfere significantly with the "blanching" sign.

Six roentgenograms; 2 charts; 3 tables.

ZAC F. ENDRESS, M.D.  
Pontiac, Mich.

**Patent Ductus Arteriosus with Pulmonary Hypertension Simulating Ventricular Septal Defect: Diagnostic Criteria in Ten Surgically Proven Cases.** Juan L. Gonzalez-Cerna and C. Walton Lillehei. *Circulation* 18: 871-882, November 1958. (University of Minnesota Medical School, Minneapolis, Minn.)

The authors report 10 surgically treated cases of patent ductus arteriosus in which the preoperative findings were suggestive of a ventricular septal defect. These illustrate the difficulty of diagnosing a patent ductus in the presence of pulmonary hypertension. Murmurs, thrills, and even catheterization findings become atypical. The aorta is large and pulsates vigorously instead of being hypoplastic as in patent ductus without pulmonary hypertension.

The various signs that the authors have found valuable in achieving a correct differential diagnosis are summarized in the accompanying table.

As a result of their experience, the authors make it a practice, when surgery is undertaken for ventricular



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	Patent Ductus Arteriosus Significant if present	Ventricular Septal Defect
History of rubella in first trimester of pregnancy		
Peripheral pulses	Bounding	Soft
Blood pressure	Increased pulse pressure	Decreased pulse pressure
Size of aorta	Enlarged	Hypoplastic
Retrograde aortogram	Usually positive	Negative

septal defects, to explore the ductus area. Fourteen per cent of such patients have been found to have a patent ductus, in most cases unsuspected preoperatively. Division of these large, short and thin-walled ducti is made easier by the use of new vessel relaxants which reduce both pulmonary and systemic blood pressures. Three roentgenograms; 5 tables.

ZAC F. ENDRESS, M.D.  
Pontiac, Mich.

**The Role of Angiocardiography in the Surgical Treatment of Massive Pericardial Effusions.** Cranston W. Holman and Israel Steinberg. Surg., Gynec. & Obst. 107: 639-647, November 1958. (New York Hospital—Cornell Medical Center, New York, N. Y.)

Angiographic studies in 4 of 5 patients with massive pericardial effusion established the presence and location of increased pericardial fluid and excluded mediastinal and pericardial masses. Opacification of the cardiac chambers permitted their differentiation from effusion and contributed to an understanding of the bizarre contours of the cardiac silhouette in terms of fluid location. The authors state:

"Observations following angiocardiography reveal that the pericardial effusions first begin in the infracardiac, diaphragmatic portion of the pericardium. As fluid increases, the retrosternal pericardial space is filled and can often be recognized by eliciting dullness over the sternum. In pericardial effusions, the heart is surrounded by fluid, except posteriorly, where pericardial reflections over the inferior vena cava below and the pulmonary veins, pulmonary artery and aorta above, prevent accumulation of fluid. Because of the retrosternal pericardial accumulation of fluid, the blood-filled cardiovascular structures are forced backward, compress the lung and bronchi and are responsible for Ewart's sign [bronchial breathing and dullness on percussion at the lower angle of the left scapula in pericardial effusion]. In massive pericardial effusions marked distention of the lateral pericardial pouches occurs and behaves like inflated water wings, causing additional compression, thus enhancing Ewart's sign."

In the 5 cases reported recovery promptly followed decompression, drainage, and pericardiectomy. In pericardial paracentesis, in order to avoid traversing the lung, the authors suggest the anterior route in the region of the xiphoid or apex of the heart.

The radiographic illustrations (21) are excellent.

MORTIMER R. CAMIEL, M.D.  
Brooklyn, N. Y.

**Aortic Valvular Diseases Studied by Percutaneous Thoracic Aortography.** Per Ödman and Jan Philipson. Acta radiol. Suppl. 172, 1958. (Södersjukhuset, Stockholm, Sweden)

This monograph summarizes findings in 17 normal and 21 abnormal cases, so evaluated according to the absence or presence of defects in the appearance of the valvular apparatus or the streaming situation in the ascending aorta. The normal cases included 12 of coarctation of the aorta. Only 3 of the abnormal cases could not be definitely diagnosed. The authors precede the account of their own studies by a brief review of earlier investigations.

**Method:** The polythene catheter is specially designed with a small distal hole and three side holes directed obliquely backward. Its distal 10 cm. is curved better to fit the aortic arch. The catheter is introduced percutaneously through one of the femoral arteries and placed in the middle segment of the ascending aorta. Approximately 1 ml. per kilogram of body weight of contrast material is injected at the rate of 15 to 20 ml. per second. To keep the aortic cusps from projecting over the vertebral column a slight left anterior oblique position is used. Films are made simultaneously at right angles to each other at a rate of 6 per second with an exposure time of 0.04 second or less. To eliminate irrelevant movement the patients are anesthetized and kept in apnea during the exposure series.

**Normal:** During systole the cusps unfold rapidly sideways and stand parallel to the aortic wall while the blood pumped from the left ventricle intrudes upon the contrast media as a centrally situated cylindrical or conical area of lesser density. During diastole the cusps meet in the approximate center of the orifice and the aortic sinuses, which were relatively deep in systole, now look like shallow bulges. The thoracic aorta is subject to small variations in caliber, 2 or 3 mm. maximally.

**Aortic Stenosis** (8 cases): In aortic stenosis the valves are thickened and have restricted mobility. The defect in the contrast column caused by the blood streaming through the narrowed orifice was seen as a jet effect, resulting in varied degrees of turbulence. In addition to its characteristic dilatation, the ascending aorta may show large variations in diameter depending upon the cycle.

**Aortic Insufficiency** (8 cases): In aortic insufficiency there was regurgitation of contrast material into the left ventricle, the severity of the condition being based on (1) rapidity of reflux, (2) amount of retention following injection, and (3) degree of dilatation and evacuating capacity of the left ventricle. The thoracic aorta is dilated, again with great variations in caliber between systole and diastole.

**Combined Stenosis and Insufficiency** (2 cases): When stenosis and insufficiency are both present, the findings are similar to those in pure stenosis, with the addition of reflux into the left ventricle. The reflux, however, is typically less in degree than in predominant aortic insufficiency.

The reproductions of roentgenograms illustrating the authors' findings are quite good but, with subject matter having such a gradual density gradient, detail is invariably lost and the reader must at times rely heavily on the identifying arrows.

Fifty-six roentgenograms; 2 diagrams; 1 graph.

HOWARD J. BARNHARD, M.D.  
Hahnemann Medical College



**Abdominal Aortography.** Owings W. Kincaid and George D. Davis. *New England J. Med.* **259**: 1017-1024, Nov. 20, 1958; 1067-1073, Nov. 27, 1958. (Mayo Clinic, Rochester, Minn.)

This treatise on abdominal aortography is in two parts and consists in a comprehensive review of the literature, with an extensive up-to-date bibliography. Following an historical introduction, the varying techniques are discussed, and indications for the procedure in the light of present-day advances in vascular surgery and urology are covered in detail. Complications are reviewed, including personal experience in over one thousand cases at the Mayo Clinic. A list of suggestions for the avoidance of complications is given.

This article, by its very nature, does not lend itself to abstracting. Those who are especially interested in aortography will find it worthwhile.

One table. MAJ. MARTIN A. THOMAS, M.C.  
MacDill AFB, Tampa, Fla.

**Chronic Dissecting Aneurysm of the Aorta Diagnosed by Aortography.** H. H. G. Eastcott and David Sutton. *Lancet* **2**: 73-75, July 12, 1958. (St. Mary's Hospital, London, W. 2, England)

Dissecting aneurysms of the aorta usually run a rapid clinical course and are often fatal within twenty-four hours. Occasionally, however, patients recover from the initial episode and may live for many years with the condition unrecognized. A case of chronic dissecting aneurysm of the aorta complicated by hypertension is reported. The diagnosis was made by lumbar aortography and confirmed by transfemoral aortic catheterization.

The diagnosis of dissecting aneurysm, rarely made during life, may be suggested by progressive enlargement of the aortic shadow on plain serial roentgenograms of the chest. This possibility was raised in the authors' patient on his original admission to the hospital in 1952. The sign, however, must be treated with caution and can be misleading. Great care must be taken that the serial films are exactly comparable. The use of a contrast medium will allow positive proof of the diagnosis, but few cases could be found where it had been employed. In the present case a positive and unequivocal diagnosis was made (in 1956) by contrast vascular studies: not only was the aneurysm itself directly demonstrated by lumbar aortography, but the original lumen of the aorta was clearly visualized by percutaneous catheterization from the femoral artery. The angiographic findings in this case support the opinion of Drury (*Brit. M. J.* **2**: 1114, 1955), who held that most of the patients who survive are those with a normal ascending aorta, and that most healed dissecting aneurysms begin at or near the aortic arch. He was also of the opinion that the second factor that appeared to encourage healing was the length of the aneurysm. Most healed dissecting aneurysms are long and sheath-like, extending from the arch to the iliac arteries.

Three roentgenograms.

**Renal Function After Aortography with Large Contrast Medium Doses. An Experimental Study in Dogs.** N.P.G. Edling, C. G. Helander, F. Persson, and Å. Åsheim. *Acta radiol.* **50**: 351-360, October 1958. (Karolinska Sjukhuset, Stockholm, Sweden)

Renal function before and after large contrast medium doses in aortography was investigated in 8 healthy dogs.

For this purpose Inulin and PAH (paraminohippuric acid) clearance studies were carried out. In each instance, the contrast material was injected with the tip of the catheter positioned in the aorta 2 to 3 cm. above the level of the renal arteries. The dose of contrast material was relatively five times as large as the amount usually injected into the human aorta, and a marked nephrographic effect was noted in each instance.

The clearance studies indicated no impairment of renal function in any of the dogs. All of the animals were sacrificed four days after the aortogram, and pathologic examination of the kidneys revealed no abnormalities.

Renal damage in aortography has been reported in the literature, but in these cases there was evidence of impaired renal function prior to aortography or a direct injection of contrast material into a renal artery was responsible for the injury. In some instances of renal failure when a proper technic had been used, renal function had not been evaluated before injection.

The results in this experiment seem to indicate that properly performed aortography will not damage healthy kidneys in human subjects.

Two roentgenograms; 2 diagrams; 1 table.

SAMUEL B. HAVESON, M.D.  
University of California, S.F.

**Five Year Observations on Unsupported Fresh Venous Grafts of the Aorta in Dogs.** John E. Jesseph, Thomas W. Jones, Lester R. Sauvage, Edmund A. Kanar, Lloyd M. Nyhus, and Henry N. Harkins. *Surg., Gynec. & Obst.* **107**: 623-630, November 1958. (University of Washington School of Medicine, Seattle, Wash.)

Autogenous vein grafts were successfully implanted in aortas of 4 dogs, which were kept under observation for more than five years before sacrifice. All grafts were evaluated for dilatation by periodic aortography at intervals of several months to a year. For this procedure the dogs were lightly anesthetized with Nembutal and the contrast medium (Diodrast or Urokon) was injected through a catheter passed into the aorta through either a brachial or femoral artery. In each instance the impressions obtained from the aortograms were confirmed by the gross examination of the excised grafts obtained when the animals were sacrificed.

The functional result in all the grafts was excellent, with no instance of occlusion or rupture. Dilatation of varying degree occurred in 3 of the 4 grafts. In each instance this was seen early in the five-year period of observation and was not progressive.

Four roentgenograms; 3 photomicrographs; 7 photographs. MORTIMER R. CAMIEL, M.D.  
Brooklyn, N. Y.

**Partial Anomalous Pulmonary Venous Drainage.** O. Fiandra, A. Barcia, R. Córtes, R. López Soto, J. Stanham, and M. Lombardero. *Acta radiol.* **50**: 460-467, November 1958. (University Hospital, Montevideo, Uruguay)

The authors report the case of an asymptomatic ten-year-old boy with anomalous venous drainage from the left lower pulmonary lobe into a dilated superior vena cava. The abnormal venous trunk returned a calculated 45 per cent of the flow of the pulmonary artery to the right heart, but the only physical sign or symptom was a murmur after exertion.

Roentgen examination revealed increased vascularity of the lungs, dilatation of the pulmonary artery, widened superior mediastinum, and right heart enlargement. Presence and location of the defect were established by right heart catheterization and biplane selective angiocardiology.

Hemodynamic factors, embryology of the lesion, and differential diagnostic features are discussed.

Five roentgenograms.

MAJ. NEIL E. CROW, M.C.  
Lackland AFB, Texas

**Anomalous Drainage of All the Pulmonary Veins into the Left Innominate Vein with Interauricular Communication: So-Called Taussig-Snell-Albers Syndrome.** I. Ferrario. Schweiz. med. Wchnschr. 88: 256-261, March 15, 1958. (In German) (Pathologische Institut der Universität Zurich, Switzerland)

From among the various malformations of the pulmonary veins, the well defined entity of the Taussig-Snell-Albers syndrome can be separated. It is characterized by abnormal openings of all the pulmonary veins into the vena anomyma sinistra (left innominate vein) combined with interauricular septal defect, but without other major heart malformation.

The clinical and pathological findings in 2 cases, observed in a series of 24 congenital heart malformations, are reported. The first patient was a white female who died of congestive heart failure at the age of four and a half years. The second was a white male infant who lived for only ten days. Of 57 similar cases found in the literature, 35 were recognized at autopsy, 6 by surgery, and 16 by heart catheterization and angiography.

The malformation is due to an arrest of growth of the sino-atrial region at the end of the first month of embryonic life. This may be associated either with lack of formation or with secondary closure of a connection between the pulmonary venous system and the heart. As a consequence, there is usually a persistent anastomosis between the plexus pulmonalis and the left vena cava superior, combined with hypoplasia of the left atrium, underdevelopment of the left ventricle, and hypertrophy of the right ventricle. Sometimes, as in the author's first case, the media of the small intrapulmonary arteries is thickened. In this case also there was a congenital pericardial diverticulum in the posterior wall.

The clinical diagnosis can be presumed during the first month of life with the aid of a postero-anterior chest roentgenogram, which reveals a characteristic figure-of-eight image produced by the increased shadow of the superior mediastinum and the heart. The symptoms are dyspnea especially on exertion, cyanosis, and pulmonary congestion, associated with frequent bronchopneumonias and progressive heart failure. Electrocardiograms show hypertrophy of the right ventricle and sometimes hypoplasia of the left ventricle. The diagnosis must be confirmed by angiocardiology and heart catheterization.

The prognosis is discussed in detail. It depends on the compensatory capability of the right ventricle, the failure of which is usually responsible for death.

Surgical treatment has been attempted, but with rather disappointing results.

Eleven figures, including 1 roentgenogram.

HERBERT POLLACK, M.D.  
Chicago, Ill.

**Renal-Vein Catheterisation and Venography: A New Technique.** W. S. Peart and David Sutton. Lancet 2: 817-818, Oct. 18, 1958. (St. Mary's Hospital, London, W. 2, England)

In studies on human renal function, it is necessary to collect renal venous samples from each kidney at close intervals of time. The authors describe a new technic for bilateral renal-vein catheterization, using a catheter with a controlled tip.

An ordinary nylon cardiac catheter (No. 7, 8, or 9) is cut down to 35 cm., with the usual syringe mounting at the end. A No. 5 nylon filament is threaded to an eyeless round-bodied needle and passed through the wall of the catheter 2.5 cm. from the tip, passing from inside to outside, being secured by a single knot cut short. Next, the needle is again passed through the wall, into the lumen, 3 cm. below, and the thread is brought out of the bottom end of the catheter. The needle is then passed back through the wall of the catheter from inside to outside, just above the syringe mounting. The end of the thread is looped and traction on it will bend the tip in the required direction.



Working the nylon thread in the holes will give the necessary sliding fit, so that the catheter can resume its natural shape when traction ceases. Care must be taken to have the holes through which the thread slides only a little larger than the thread itself in order to avoid leaks.

With local anesthesia the saphenous vein is exposed below the saphenous ring; the catheter is introduced and passed upward. Under fluoroscopic control the tip of the catheter is advanced to the level of the first lumbar vertebra and traction is applied on the thread so as to bend the tip and bring it up against the lateral wall of the inferior vena cava. When the catheter is pulled down gently, maintaining traction, the tip will usually spring into the mouth of the renal vein. The thread is then released and the tip of the catheter can be advanced down the vein. On the right this will take it well out into the flank. On the left, the tip usually stops at the left vertebral margin. During all these procedures normal saline containing 1,000 units of heparin per liter is dripped through the catheter. Blood can be drawn back rapidly, unless the tip is up against the vein wall, and in that case blood will flow if the catheter is gently withdrawn. The normal renal-vein blood can be recognized by its bright red color, compared with that in the inferior vena cava.

For venography the patient performs the Valsalva maneuver immediately before the injection of 15 ml. of 70 per cent Diaginal or 70 per cent Pycosil. The contrast medium is injected as rapidly as possible, the aim being to deliver the total dose within two seconds. A roentgenogram is taken as the injection reaches its close. It is preferable to obtain several rapid serial films rather than a single film, but this was not possible with the screening table used by the authors, and a single film usually proved adequate.

Bilateral renal vein catheterization was carried out

successfully in 27 patients, with failure to enter one renal vein in 2, and failure to enter either renal vein in 1. The only complication in the series was a local thrombophlebitis in the saphenous vein in 1 patient.

Although placement of the catheter in the renal vein can be inferred by indirect observations, renal venography is the only means of obtaining accurate knowledge of the position of the catheter and of the drainage area from which the blood samples have been collected. The authors' venographic studies have shown that a catheter tip which is thought to be in the renal vein may actually be in a lumbar or testicular vein. Their studies also showed that, although renal-vein blood may form the main contribution to a blood sample on the left side, this may also contain blood from systemic and suprarenal veins. With the technic described, bilateral renal-vein catheterization has proved simpler and more consistently successful than with previous technics of approach from above.

Six roentgenograms; 1 drawing.

**Vascular Syndromes from Dilatation of Arteriovenous Communications of the Sole of the Foot.** Edmond Malan. *Arch. Surg.* 77: 783-795, November 1958. (Department of Surgical Pathology, University of Genoa, Italy)

Certain patients experience vascular difficulties, manifested by sudden onset of painful coldness over the foot, accompanied by deep burning sensation. These are usually young people, with symptoms occurring after prolonged walking or dancing. The symptoms, unlike those of intermittent claudication, disappear very slowly on rest. No vascular alterations are apparent on routine arteriographic studies or routine functional and laboratory tests, but the author has demonstrated minute arteriovenous communications in the sole of the foot by arteriography and serial filming.

The speed of arterial circulation is enormously increased, the last arteriolar branches of the foot being seen to opacify within five to six seconds instead of eleven to fourteen seconds, as is normal. It is almost constantly possible to see radiopaque maculae in the sole. These may be localized in the region of the heel or in the anterior metatarsal area, or may be more generalized. Finally, the venous network appears quite early. In some instances, even after five or six seconds it is possible to observe small veins leaving the maculae to join the major branches forming the veins of the foot and then entering the veins of the leg.

Three syndromes are described:

(1) The arteriovenous communications are supplied only by the plantar arteries, branches of the posterior tibial artery. The pain occurs with exercise and may involve the entire sole.

(2) The arteriovenous communications in the distal half of the sole are supplied by intermetatarsal perforating arteries, coming from the anterior tibial artery. The symptoms of ischemia occur in the forefoot.

(3) Arteriovenous communications are dilated in the entire sole. Symptoms involve the entire foot.

These syndromes cannot be differentiated by clinical symptoms alone, due to considerable variation of the pain, coldness, and burning sensation encountered.

Plethysmographic findings and a satisfactory method of surgical treatment are described.

Eighteen roentgenograms; 14 drawings; 2 graphs; 2 tables.

J. S. ARAJ, M.D.  
Toledo, Ohio

**Leiomyoma of the Greater Saphenous Vein with Preoperative Localization by Phlebography.** James A. DeWeese, Roger Terry, and Seymour I. Schwartz. *Ann. Surg.* 148: 859-861, November 1958. (University of Rochester School of Medicine and Dentistry, Rochester, N. Y.)

The authors report a case of leiomyoma arising in the greater saphenous vein with extension into the common femoral and external iliac veins, in which phlebography was of great value in determining the exact location and extent of the tumor preoperatively.

Twelve cases of tumors arising from the vein wall were found in the literature. In 8 of these cases, the determination of the exact origin of the tumor was difficult. However, they were accepted as being probably of venous origin.

Three figures, including 1 roentgenogram.

RAUF YAGAN, M.D.  
Cleveland Metropolitan General Hospital

**Tilt Phlebography: A Reliable Method for Diagnosing Incompetent Communicating Veins.** Frits R. Mathiesen. *Acta radiol.* 50: 430-443, November 1958. (Rigshospitalet, Copenhagen, Denmark)

The author describes a modified technic of tilt phlebography for demonstrating incompetent communicating veins in the lower extremity. This he has employed in 687 examinations in 470 patients, with no complications. He believes it to offer advantages over retrograde phlebography, which, in the presence of normal valves in the deep veins, affords no information regarding the communicators.

Bearing in mind the method of tilt phlebography recently described by Dohn (*Acta radiol.* 50: 293, 1958. *Abst. in Radiology* 73: 137, 1959), the author based his modifications on the following considerations: (1) rapidity of injection of the medium (40 c.c. in ten to twenty seconds), which necessitates the application of a tourniquet about the malleoli and the use of a stout venous needle; (2) tilting of the table to a horizontal position following venipuncture, and restriction of loss of blood by compression over the puncture site; (3) two sets of films in the same projection in order to demonstrate the direction of filling of the communicating veins in the erect posture; (4) completion of exposures within half a minute after tilting; (5) compression of the great saphenous vein by a tourniquet.

Twenty-four roentgenograms; 1 photograph.

MAJ. H. H. STURTEVANT, M.C.  
Lackland AFB, Texas

## THE DIGESTIVE SYSTEM

**X-Ray Examination of the Esophagus.** Frederic E. Templeton. *Gastroenterology* 35: 498-503, November 1958. (455 Medical-Dental Bldg., Seattle, Wash.)

This paper gives a rather detailed description of the author's fluoroscopic and filming procedure for examination of the esophagus. It does not lend itself well to abstracting but is recommended in its entirety to those who are beginning their training in gastrointestinal radiography and to those wishing to improve their technic in evaluating the esophagus.

Some generalized conclusions are drawn. The author believes, for instance, that both fluoroscopy and films properly exposed during and after fluoroscopy are necessary for adequate examination of the esophagus. He

does not believe in excessive diagnostic procedures along with the procedure.

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does not believe in haphazard filming nor does he believe in excessive fluoroscopy without films. Representative diagnostic films decrease the dose of radiation and, along with fluoroscopy, constitute the recommended procedure.

J. P. CHAMPION, M.D.  
Grand Rapids, Mich.

**A Comparison Between Radiology and Oesophagoscopy in the Investigation of Reflux Oesophagitis.** Martin Spiro. *Brit. J. Radiol.* 31: 626-630, November 1958. (Connaught Hospital, London, E. 17, England)

One hundred cases of reflux esophagitis diagnosed clinically were studied and a comparison was made between radiology and esophagoscopy in establishing the diagnosis. Radiological diagnosis of esophagitis presented a difficult problem and in many cases could not be made with certainty. Esophagoscopy, on the other hand, showed the characteristic inflammatory state of the mucosa in all 65 cases in which that examination was carried out. In only 13 of these were typical mucosal changes demonstrable radiologically. Direct vision was also more accurate in finding small flat ulcers, but the two types of examination were complementary in the detection of most peptic ulcerative changes of the esophagus. Gastroesophageal reflux was better seen at x-ray study, as was the hiatus function during swallowing. Roentgenography was needed to demonstrate the length and tortuosity of the area of narrowing and the degree of obstruction in cases of esophageal stricture.

X-ray criteria for the diagnosis of esophagitis are listed:

- (1) Early, indirect: Spasm, abnormal peristalsis, delay in emptying.
- (2) Direct signs: Coarsened and thickened rugae, broadening and loss of definition of the mucosal pattern.
- (3) Later signs: Persistent irregular narrowing. The most common cause of reflux esophagitis was hiatus hernia.

Fourteen roentgenograms; 2 tables.

MAJ. H. N. STURTEVANT, M.C.  
Lackland AFB, Texas

**The Radiologic Aspects of Progressive Scleroderma.** J. Pasquier. *Schweiz. med. Wchnschr.* 88: 1237-1240, Dec. 6, 1958. (In French) (Institut Universitaire de Radiologie, Lausanne, Switzerland)

After a review of the literature, the author describes the roentgen findings in 5 cases of progressive scleroderma. Because of the frequency of difficulty in swallowing, the esophageal lesions are especially emphasized. These may vary from a simple dyskinesia to marked megaesophagus. Cardiospasm, inflammation of the esophagus, and ulcerous or submucous carcinoma must be considered in the differential diagnosis.

Twelve roentgenograms.

**Barium Meal and Follow-Through.** A. C. Glendinning. *Lancet* 2: 664-667, Sept. 27, 1958. (Bromley Group of Hospitals, Kent, England)

Haudek, in 1912, made the observation that, if there was a considerable residue in the stomach six hours after a contrast medium meal, this was good evidence that a disorder was present. This concept has persisted through the succeeding years. In modern practice the six-hour residue is linked with the idea of a barium meal and follow-through; when performed in a routine

way, this examination is likely to prove unsatisfactory. Between August 1949 and April 1951, the author studied a large series of cases in an attempt (1) to determine the percentage of cases in which there appeared to a "significant" six-hour residue and (2) to gain further insight into the true place of the follow-through in gastrointestinal examination. In all, 1,000 barium meals were given and, with allowances for re-examination, 866 patients (439 males, 427 females) were seen. All were screened before and during the ingestion of the meal. Five basic radiographs were taken (2 erect, an erect serial of the duodenal cap, 1 supine, 1 prone), with additional films as indicated. All patients were screened again after an hour, and roentgenograms were taken at six hours.

Ninety-eight males and 117 females were found to have a significant residue after six hours, and these 215 patients were later traced and re-examined if possible, some as late as 1957. Eleven patients had died, and 32 could not be located. Three patients, still suffering from dyspepsia, refused examination. Seventy patients had no dyspepsia or were normal on a repeat barium meal study; 52 had chronic peptic ulcer; 32 had had partial gastrectomy for peptic ulcer; 15 had other gastrointestinal lesions proved at operation. Of the total followed up, 38.2 per cent were regarded as not having any significant upper gastrointestinal abnormality. The percentage of males in whom findings were normal was little more than half the comparable percentage in females. This is probably no more than an echo of the fact, demonstrated by the initial examinations, that slow stomach emptying is more of a female than of a male characteristic.

In the final analysis, Haudek may be said to be broadly supported by the results of this investigation. Organic disease, especially peptic ulceration, leads to slow emptying because of either spasm at the pylorus or stenosis. Slow emptying of the stomach is found also in another group of patients, those with the normal hyposthenic type of stomach, but with a relatively immobile high duodenal cap—a cap, in fact, in the position usually described in textbooks of anatomy. If these patients are up and about, emptying may be very slow; it occurs readily in the recumbent position, especially prone and oblique. From the point of view of everyday practice, it is important to know that delayed emptying from whatever cause can usually be recognized at the initial examination or, failing this, within an hour. Further radiographs to prove the obvious are unnecessary. The author believes that little help toward a diagnosis is ever likely to come from screening or films at one hour or at six hours. Furthermore, when the follow-through is carried on to twenty-four or forty-eight hours, it is usually equally disappointing. The examination is wasteful of time, energy, and material, and might well be abandoned as a routine test.

Two charts; 2 tables.

**The Prepyloric Contractions in Certain Abnormal Conditions.** A. D. Keet, Jr. *Acta radiol.* 50: 413-429, November 1958. (Groote Schuur Hospital, Cape Town, Union of South Africa)

This is the second report by the author on a study of 700 gastrointestinal series. The first described the prepyloric contractions in 310 normal cases (*Acta radiol.* 48: 413, 1957. *Abst. in Radiology* 71: 611, 1958). This report concerns 390 abnormal cases.



These are classified as (1) simple spasm, including antral gastritis, (2) spasm with an organic lesion elsewhere in the stomach or duodenum, (3) spasm with prepyloric ulcer, (4) pylorospasm, (5) adult hypertrophic pyloric stenosis, (6) focal hypertrophy of the lesser curvature "muscle knot," (7) mucosal prolapse, and (8) pyloric carcinoma.

Fifteen roentgenograms; 1 drawing.

MAJ. H. N. STURTEVANT, M.C.  
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#### Perforation of the Stomach in the Newborn.

Richard B. Magee and R. Marvel Keagy. *Pennsylvania M. J.* 61: 1204-1206, September 1958. (1308 9th St., Altoona, Penna.)

A case of spontaneous gastric perforation in a 7-day-old white female is presented. In diagnosis of the condition the use of contrast media is unnecessary and wasteful of time. Upright films of the abdomen demonstrate free peritoneal air, often free peritoneal fluid, and absence of the "gastric bubble." With roentgen evidence of pneumoperitoneum, immediate surgery is imperative.

Two roentgenograms.

**Carcinoma of the Gastric Stump After Resection for Benign Peptic Ulcer.** Ch. Debray, M. Bouvry, and P. Roches. *Schweiz. med. Wchnschr.* 88: 631-634, June 28, 1958. (In German) (Hôpital Bichat, Paris, France)

Up to about twenty years ago the occurrence of a primary carcinoma in the gastric stump after resection for a benign ulcer was considered a rare incident. It appears, however, to be much more frequent than was formerly believed. The authors review 113 cases, including 11 of their own. In all of these the benignity of the ulcer was definitely established and a free interval of at least five years had elapsed between gastrectomy and the onset of cancer symptoms. Cases of palliative resection and simple gastroenterostomy, where the ulcer was left *in situ*, with the possibility that it may have undergone malignant change, are not included.

The average interval between resection and the onset of symptoms was fifteen years. The clinical manifestations are dependent upon the location of the carcinoma, which may arise at either the enterostomy site or at the cardia. The patients usually complained of pain shortly after food intake. Vomiting was frequent, suggesting a stenosis at the gastroenterostomy. Anorexia was invariably present. Dysphagia, which was observed in 5 of the authors' 11 patients, usually points toward neoplastic invasion of the cardiac portion. Hematemesis was only infrequently observed. Deterioration of the general condition, with loss of weight, asthenia, and anemia, was among the early symptoms.

The authors state that resection for a gastric ulcer almost triples the incidence of cancer and give three etiologic factors for the stump carcinoma: (1) ulcer degeneration, (2) acidity, and (3) structural changes of the mucosa. They recommend taking into consideration a primary stump carcinoma whenever late complications occur after gastric resection, especially for gastric ulcer. The diagnosis is made by roentgenography and gastroscopy. The prognosis is poor.

Five roentgenograms. HERBERT POLLACK, M.D.  
Chicago, Ill.

**Incarceration of the Stomach and Intestine After Traumatic Rupture of the Diaphragm.** F. Kümmerle. *German M. Monthly* 3: 346-347, November 1958. (Chirurgische Universitätsklinik, Freiburg/Br., Germany)

Among 15 cases of traumatic rupture of the diaphragm coming under the author's care during the last six years, incarceration of the stomach was observed once and of the colon twice. In all 3 cases, the presence of a hernia was revealed only after incarceration had occurred, being demonstrated by x-ray examination. A transthoracic approach was employed at surgery. Two of the patients did well postoperatively; 1 died on the sixteenth postoperative day of a pulmonary embolus, although at the time of death the intestinal suture was healed and functioning.

A review of the literature revealed the following facts. The incidence of strangulation in traumatic diaphragmatic hernias varies from 15 per cent in the older accounts to 95 per cent in more recent reports. About 98 per cent of cases occur on the left side. The mortality of strangulated hernias is high if perforation occurs, figures varying from 30 to 88 per cent. Frequently, the presence of traumatic hernia is revealed only after incarceration has occurred, as in the author's 3 cases. The time interval between rupture and obstruction ranges from a few weeks to many years.

Five roentgenograms; 1 drawing.

RAUF YAGEN, M.D.

Cleveland Metropolitan General Hospital

**Intussusception in Infancy and Childhood. An Analysis of Seventy-Seven Cases Treated by Barium Enema.** Mark M. Ravitch. *New England J. Med.* 259: 1058-1064, Nov. 27, 1958. (Johns Hopkins University School of Medicine, Baltimore, Md.)

The author states, on the basis of his clinical experience together with the even greater experience of Scandinavian and Australian authors, that hydrostatic pressure with barium enema under fluoroscopic control is the safest and most effective way of reducing intussusception.

As soon as the diagnosis is suspected, the operating room is notified and the patient formally posted for operation. Intravenous infusions of fluids are begun and the stomach is emptied and the gastric tube left in place. An ungreased 45-ml. Foley catheter is inserted into the rectum fully inflated and the buttocks are taped tightly together. The barium can is between 3 and 3 1/2 feet above the table. Anesthesia is not employed. Barium is allowed to run in without interruption.

There is a great deal of variation in the rapidity with which the intussusception is reduced. In some cases there is complete reduction almost immediately. In others forty-five minutes to an hour is required. An absolute arrest in the barium column for about ten minutes is considered indication for immediate surgery. Even with slight progress, however, one should persist.

The successful reduction of an intussusception is indicated by the following criteria: the entrance of barium well into the small bowel; the return of the barium with feces or with flatus; disappearance of the mass; clinical improvement; subsequent recovery in the stool of charcoal given by mouth.

The position of the apex of the intussusception, its duration, or the age of the patient appear to have little to do with the likelihood of successful reduction by bar-

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ium enema. In a series of 77 cases complete reduction was achieved in 58 or 75 per cent.

The author reports that in a series of 199 cases specific causes for intussusception, like Meckel's diverticulum and polyp, were found in only 6.5 per cent. These occur usually but not always in older children, *i.e.*, beyond two years of age.

Experience indicates that with a hydrostatic pressure of 3 to 3½ feet gangrenous bowel will not be reduced and perforation will not occur.

In 77 non-operated cases there were 3 recurrences which is comparable to the rate in large operative series. The risk of postoperative mechanical bowel obstruction due to adhesions is, of course, avoided. In all of the large operated series reported, several children had this complication.

Barium enema reduction of intussusception is a surgical procedure performed by surgeons while the operating room is held in readiness.

It is recommended that this article be read in the original by those concerned in the diagnosis and treatment of intussusception.

Five roentgenograms; 1 diagram.

MAJ. MARTIN A. THOMAS, M.C.  
MacDill AFB, Tampa, Fla.

#### Diagnostic Implications of the Ileocecal Valve.

Stanley Stark. *Gastroenterology* 35: 485-497, November 1958. (Beth El Hospital, Brooklyn, N. Y.)

The author reviews in considerable detail the anatomy and physiology of the ileocecal valve and adjacent regions. The radiography of this area is described with particular emphasis on the frequency with which the ileocecal valve can be seen using compression spot films and double-contrast studies. It was best demonstrated in a lateral profile projection with the patient slightly rotated to the right, and in the anteroposterior (on-end) projection with the patient slightly rotated to the left when lying supine. The on-end view resembles a round or oval dish or a wheel with spokes radiating from the center. When the patient is rotated, the valve becomes more oval at one end and pointed at the other until the profile view is obtained. The profile view appears somewhat triangular, with the apex pointing toward the cecum. The normal, rather wide range in size of the valve is mentioned and the author states that size alone is not a criterion for diagnosis of abnormality as long as the contours of the lips are smooth. In his opinion, the chief reason for being familiar with the ileocecal valve area is to recognize it as being normal, even when clearly outlined and of larger size than is ordinarily seen, to prevent needless surgery in this region.

Several illustrations of good quality demonstrate the variations in size of the ileocecal valve and, in particular, the variation in size in the same individual spot films as shown on conventional distance films.

Twenty-five roentgenograms; 1 photograph.

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**Mucocele of the Appendix, with Special Reference to Diagnosis with Double Contrast Method.** P. Bertil Norberg and Bruno Samenius. *Acta chir. scandinav.* 115: 306-311, 1958. (P.B.N., Department of Surgery I, Sahlgrenska Sjukhuset, Gothenburg, Sweden)

Mucocele of the appendix is a benign condition as

long as it is confined to that organ. The mucocele may rupture, however, pouring its contents out into the peritoneal cavity and giving rise to pseudomyxoma peritonei. It is the seriousness of this complication that makes a preoperative diagnosis of appendiceal mucocele important.

Two cases are reported in which the diagnosis was suspected on the basis of roentgen examination by the double-contrast technic. The method employed is that described by Andrén, Frieberg, and Welin (*Acta radiol.* 43: 201, 1955. *Abst. in Radiology* 66: 140, 1956). The authors believe this is particularly valuable in patients with chronic intermittent pain in the right lower quadrant of the abdomen.

Four roentgenograms; 1 photograph; 1 drawing.

**Movements of the Common Bileduct in Man. Studies with the Image Intensifier.** W. Burnett and R. Shields. *Lancet* 2: 387-390, Aug. 23, 1958. (University of Glasgow, Glasgow, Scotland)

For many years the means by which bile enters the duodenum has been of great interest to the physiologist and the clinician. Most studies, however, have been concerned with the mechanism of emptying of the gallbladder and its functional relationship with the sphincter at the distal end of the common bile duct. Little attention has been paid to any active part which might be played by the common duct, which is usually considered to be a transmitting tube with a wall mainly composed of fibrous tissue.

The authors examined with an image intensifier the biliary tract of 10 patients one or two weeks after cholecystectomy or choledochotomy. A water-miscible contrast medium, 50 or 70 per cent sodium acetrizate, was instilled at the rate of 1 ml. a minute into the common duct. The injection was made through a ureteric catheter which had been inserted at operation for a distance of about 1 cm. into the common duct through the stump of the cystic duct. If the common bile duct had been explored, the injection was made through a short T-tube left in the duct at operation. An initial injection of 3 ml. was made. Screening was done at this time to observe the filling of the duct. As the duct emptied into the duodenum, further increments of the same or less volume were instilled, the amount being determined by the rate of emptying. No discomfort was experienced by the patient, and no distention of the common duct was allowed to take place. Observations were made both during the injection and afterward. After five to ten minutes for stabilization of conditions in the duct, permanent records were made on 35 mm. film by cineradiography, with a built-in "Arriflex" camera so arranged that screening and cineradiography could be done simultaneously.

Four different types of movement were observed in the common bile duct and the related portion of the duodenum:

**Peristalsis of the Common Duct:** Waves of peristalsis in the common duct were observed in all 10 patients studied, whether or not the duct was intact or had been explored previously. The peristaltic waves traveled toward the duodenum at the rate of 3 to 5 or more a minute and lasted one to three seconds. On one occasion 5 waves were seen in thirty-six seconds. Sometimes a minute or more elapsed without a contraction. Not all the waves were complete and brought medium into the duodenum; some were abortive,

ending near the sphincter. But when a wave traveled the whole length of the duct, the medium was ejected forcibly into the duodenum, and a successful complete wave was usually followed by several more.

**Respiratory Movement:** The whole biliary tree moves with each respiratory excursion; a downward movement in inspiration is followed by a return upward movement in expiration. The bile duct and the duodenum move together, but the ejection of contrast medium into the duodenum is not in any way associated with these movements.

**Transmitted Arterial Pulsation:** In a patient with a thin abdominal wall, it was possible to see, on screening, that the common duct pulsates synchronously with the aorta. This is not surprising, because the aorta and celiac axis are close to the duct, and the hepatic artery runs in intimate relationship with the duct; hence transmitted pulsation may be expected. This movement is of minor degree and has no bearing on the emptying of the duct.

**Associated Duodenal Movements:** A study of duodenal movements in relation to the observed peristaltic and respiratory movements of the common duct was possible after some of the contrast medium had entered the duodenum from the duct. As described above, the duodenum and the common duct move together during respiration. In addition, forward and reverse peristalsis is clearly seen in the duodenum itself. No evidence was found that this peristalsis plays an active part in emptying the duct.

As a result of their study, the authors believe that the common duct functions as an actively contracting duct rather than as a passive transmitter of bile. This concept may modify current views on the genesis of biliary pain and permit the consideration of common duct colic as an entity similar in nature to ureteric and intestinal colic. It is believed, also, that there is sufficient muscle in the wall of the bile duct to produce the rhythmic movements observed.

Nine roentgenograms; 1 photomicrograph.

**Significance of Peroperative Cholangiography in the Management of Gallbladder Disease.** P. A. Ykelenstam. Arch. Surg. 77: 684-688, November 1958. (St. Canisius Hospital, Nijmegen, Netherlands)

The therapeutic significance of peroperative cholangiography is still a matter of dispute, the major objections to its use being high incidence of diagnostic errors and prolongation of operative time. In the author's opinion, cholangiography is a reliable diagnostic aid in establishing the presence of calculi in the bile ducts and strictures. Its reliability may be increased by an adequate technic and experience in interpreting the roentgenograms.

The technic described by the author minimizes air bubble introduction. A bulb-tipped needle is introduced into the cystic duct through a small transverse incision and fixed by ligature. As soon as bile starts to flow from the needle, the syringe, filled with a water-soluble opaque medium, is attached and the injection is begun. The patient's left side is elevated slightly.

The author reports the results in 100 cases that underwent preoperative cholangiography and cholecystectomy, and compares these with 100 cases in which cholecystectomy was performed without cholangiography. In the first group conventional indications for exploration of the biliary tract (as outlined by Lahey) were present in 64 cases. In 19 of these cholangi-

ography gave positive findings and exploration was undertaken in 15. Unnecessary exploration was thus avoided in a large number of cases. An important point is that in the cases where there was no clinical indication for exploration of the bile ducts, 5 showed calculi on cholangiography. In the group of patients in whom cholangiography was not done, exploration was indicated clinically in 56. Fifty of these were explored, and 48 had T-drainage. Calculi were found in 27, and 23 therefore had unnecessary exploration.

The author's arguments for peroperative cholangiography appear valid in that unnecessary exploration of the bile duct and T-drainage can be decreased, and patient morbidity can thus be cut down. The conventional indications for exploration or their absence are not as accurate for diagnosis of biliary tract disease as peroperative cholangiography.

Three tables.

J. S. ARAJ, M.D.  
Toledo, Ohio

**False Negative Shadows in Intravenous Cholangiography.** Eric Samuel and Walter Scott. Brit. J. Radiol. 31: 631-633, November 1958. (W. S., Johannesburg, Union of South Africa)

Gas bubbles in the common bile duct may produce negative shadows mimicking stones. Air in the biliary system usually indicates an internal biliary fistula, but gas may also ascend into the biliary tree when no fistula is present, as a result of malfunction of the sphincter of Oddi, or of cholecystoduodenostomy or jejunostomy. Two cases are presented. In one patient who had previously undergone a cholecystoduodenostomy (erroneously reported as a cholecystectomy) barium administered orally was seen to flow into the gallbladder and along the bile duct, outlining the path taken by the gas. The other patient was found on exploration to have an unusually atonic sphincter of Oddi.

The authors recommend a preliminary scout film, since this should show air visible in the cholangiogram. Multiple rounded defects suggest air; multiple stones are usually faceted.

A barium meal examination will confirm the presence of an internal biliary fistula when it exists, but may be of less value when no such fistula is present. Reflux of barium into the biliary tree along the fistulous track will, however, enable the diagnosis to be confirmed.

Four roentgenograms.

CAPT. HARRIS W. KNUDSON, M.C.  
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## THE SPLEEN

**Rupture of the Spleen in Newborn Infants. Recovery after Splenectomy.** William K. Sieber and Bertram R. Girdany. New England J. Med. 259: 1074-1076, Nov. 27, 1958. (Children's Hospital of Pittsburgh, Pittsburgh, Penna.)

The authors report 3 cases of splenic rupture in newborn infants with prompt diagnosis, splenectomy, and survival. The important diagnostic features are signs of blood loss, with abdominal distention. Abdominal films which showed the classic signs of free fluid in the peritoneal cavity were obtained in all 3 patients. The mechanism of the splenic rupture in these cases is not explained.

Previous papers state that bleeding from the liver is the most common cause of hemoperitoneum in the

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newborn. No case of ruptured liver, however, has been seen at the authors' hospital since 1951.

Three roentgenograms.

MAJ. MARTIN A. THOMAS, M.C.  
MacDill AFB, Tampa, Fla.

## THE MUSCULOSKELETAL SYSTEM

### Albers-Schönberg's Disease; Report of 2 New Cases.

J. Bodart. *J. belge de radiol.* 41: 645-680, 1958. (In French)

This is a review based on the study of 115 cases of Albers-Schönberg disease from the medical literature and 2 personal cases. The clinical picture consists in anemia, fragility of the bones, maxillary osteitis, and optic atrophy. Occasionally there may be an association with other syndromes, such as cleidocranial dysostosis.

The roentgen picture ranges from more or less generalized symmetrical homogeneous osseous condensation to discontinuous forms showing parallel striations in the metaphyses of the long bones and concentric rings in the short bones. In some of the long bones the shaft may be of normal width and appear to enlarge abruptly near the extremity, giving rise to "clubbing." Occasionally the roentgen appearance suggests the presence of bone within a bone.

Five roentgenograms; 1 table.

CHARLES M. NICE, JR., M.D., PH.D.  
Tulane University

**Dyschondroplasia with Multiple Hemangiomas (Maffucci's Syndrome).** Kurt Marberg, Fritz Dalith, and Harry Bank. *Ann. Int. Med.* 49: 1216-1228, November 1958. (Government Hospital, Tel-Hashomer, Israel)

Maffucci's syndrome consists of a combination of dyschondroplasia of Ollier and multiple hemangiomas. The latter are more obvious in the subcutaneous tissues and mucous membranes, but apparently can occur in the internal structures as well. Vascular changes may be associated, namely, phlebectasia and lymphangioma. In the case reported in this communication there were lymphangiectatic changes in the skin.

The lesions appear early in life and generally progress up to the end of the growth period. The uneven growth of bone leads to gross skeletal deformity and frequent fractures are encountered due to the defects of ossification resulting from the enchondromatosis. This condition is not inherited and does not appear to have any particular geographic or racial distribution. Its etiology is not known but it is probably the result of multiple defects in a single gene.

The authors' case is believed to be the thirty-fifth reported in the literature. Their patient was a woman of forty with pronounced bony changes and extensive hemangiomas. Lymphangiomas were also proved in this patient by biopsy and there were various changes in pigmentation. It was the feeling of the authors that these latter had their origin in the vascular lesions.

The accompanying photographs and radiographs demonstrate well the characteristic features of this unusual condition.

Four roentgenograms; 1 photomicrograph; 4 photographs.

J. A. GUNN, M.D.  
Grand Rapids, Mich.

**So-Called Spontaneous Cervical Dislocations. A Clinical, Roentgenological, Surgical and Post-Mortem Study of the Pathogenesis and Treatment in Five Cases.** Tormod Hauge. *Acta chir. scandinav. Suppl.* 232, 1958. (Rikshospitalet, Oslo, Norway)

Five cases of spontaneous or non-traumatic cervical dislocation are reported. In each instance the clinical findings, the interpretation of the roentgenograms, the observations during operation, and the autopsy findings are correlated with the experiences of other authors.

In 3 cases the dislocation was localized to the atlanto-axial joints. In 1 of these a separated odontoid process was demonstrated roentgenologically; in the other 2 assimilation of the atlas was found, with fibrous thickening of the dural fold in the foramen magnum, *i.e.*, congenital occipito-cervical anomaly. In 1 case symptoms of dislocation appeared in connection with trauma of the head and recurred three years later following a throat infection. One patient arrived for treatment twelve years after an attack of rheumatic infection. In the interval several relapses with symptoms of progressive cervical dislocation had occurred. In the third case the onset of the disease was associated with a chronic polyarthritis and complicated by symptoms of grave myelopathy.

Autopsy was performed in 2 of the cases of atlanto-axial dislocation. The cause of the dislocation was chronic destructive inflammation, which in 1 case was of a specific rheumatic nature. This chronic inflammation is shown to be destructive to muscles, ligaments, joint ligaments, joint surfaces, bones, and intervertebral disks. Neuro-anatomical studies were made in the case with myelopathy. The origin of the myelopathy is tentatively ascribed in part to purely mechanical factors, but the possibility of a congenital involvement of the nervous system in cases of occipito-cervical anomaly is discussed.

In 2 cases the dislocation occurred in the more caudal parts of the cervical column, in 1 associated with chronic polyarthritis and in the other with rheumatoid spondylitis. Both patients had severe neurological symptoms. In these cases also the cause of the spontaneous dislocation was a chronic destructive inflammation.

On the basis of his own experience and that of others, the author believes that a spontaneous cervical dislocation should always be regarded as a potentially progressive condition, which sooner or later may lead to neurological symptoms.

Recommendations as to treatment are made.

Eight roentgenograms; 4 photomicrographs; 5 photographs.

**The Vertebral Pedicle Sign: A Roentgen Finding to Differentiate Metastatic Carcinoma from Multiple Myeloma.** Harold G. Jacobson, Maxwell H. Poppel, Jerome H. Shapiro, and Samuel Grossberger. *Am. J. Roentgenol.* 80: 817-821, November 1958. (Montefiore Hospital, New York 67, N. Y.)

The more common sites of skeletal involvement in metastatic carcinoma and multiple myeloma are not significantly different. Frequently, the radiologist has difficulty in distinguishing the two conditions. Studies by previous authors have suggested some differential features, as follows: (1) In spinal involvement a perispinal mass is more frequently seen with multiple myeloma than with metastatic carcinoma. (2) Osteo-

porosis is a frequently associated finding with multiple myeloma while the appearance of the uninvolved bone is usually normal with metastatic carcinoma. (3) Lytic areas in bones, particularly in the calvarium, are generally more sharply circumscribed in multiple myeloma than in metastatic carcinoma. These findings are relative and by no means infallible.

The authors have been impressed with the frequency of early vertebral pedicle involvement in the lytic type of metastatic carcinoma while with multiple myeloma the pedicles appear to be preserved until very late in the disease. They made comparative studies of films of 54 patients with proved multiple myeloma and 74 with metastatic carcinoma to the spine. Ninety-five per cent of the cases of metastatic carcinoma showed early and prominent destruction of the pedicles, frequently multiple. With multiple myeloma only 15 per cent of the patients showed pedicle destruction, and in these involvement was almost always single. Even in cases with massive skeletal invasion by myeloma the spine pedicles tended to remain relatively intact.

The authors consider the "pedicle sign" a useful differential point, carrying statistical significance. It is theorized that the reason for the differential pedicle involvement in the two diseases is related to the paucity of red marrow in the pedicles as a potential invasion site for myeloma. Why metastatic carcinoma should favor pedicle involvement remains obscure.

The points under discussion are well illustrated by 6 selected roentgenograms. Four small tables are presented.

JAMES W. BARBER, M.D.  
Cheyenne, Wyo.

**The Clinical Evaluation of Sciatica.** Carl Hirsch. *Acta orthop. scandinav.* 27: 210-218, 1958. (University of Uppsala, Uppsala, Sweden)

During the period November 1955 to January 1957, 140 patients were treated for sciatica in the Orthopedic Department of the University of Uppsala. Myelography, with a water-soluble medium, was performed in all of these patients as soon as they were admitted to the hospital, regardless of whether or not they had neurological signs. All had radiating leg pains. Myelographic findings were considered "positive" in 75 patients and "negative" in 65.

**Group I:** Forty-five patients had had radiating pain for less than two months, and in 30 of these the myelogram was considered positive (67 per cent). Surgery was advised in 26 of the 30 patients; at operation a prolapsed disk was found and removed in 25 (96 per cent). Three patients with negative myelograms were operated upon because of the severity of their pain. In 1 of these a prolapse was found; exploration of two interspaces was negative in the others.

**Group II:** Ninety-five patients had had radiating pain for more than two months, and in 45 of these the myelogram was considered positive (47 per cent). Thirty-nine of the patients with positive myelograms were operated upon; ruptured disks were found in 33 (85 per cent); in the patients with negative operative findings two interspaces were explored. Eighteen of the 50 myelographically negative cases were operated upon; in 8 a prolapsed disk was found and removed.

In 10 patients surgery was not performed, despite positive myelograms. At the time of writing, it was too early to say whether these patients will recover. Two had weakness of the foot, which disappeared to-

gether with the pain. They still suffered from numbness and had to be careful in their activities, although six to eight months had elapsed since the onset of their sciatica. In 8 patients the sciatica was still present though the pain varied in intensity. The author believes that these will require operation later.

Early myelography with a water-soluble medium tells in about 50 per cent of the cases whether or not the underlying cause of the sciatica is a ruptured disk. With early operation, patients with ruptured disks will recover more quickly and be able to resume work more promptly than if surgery is undertaken after long conservative care. Since no prolapse may be found in about 40 per cent of the cases with negative myelograms, surgery should be advised in such cases only if the pains are severe. How early should operation be performed? The author thinks that two months is an acceptable time; in patients with positive myelograms, however, it might be suggested earlier if the clinical picture warrants.

Two roentgenograms; 3 tables.

**The Radio-Opacity of Glass Foreign Bodies, with Report of a Case of Injury of the Cauda Equina by Fragments of Glass.** W. Bryan Jennett and James A. Watson. *Brit. J. Surg.* 46: 244-246, November 1958. (Cardiff, Wales)

The authors report the case of a young girl, who fell on a wine glass, with resulting penetration of glass fragments into the sacral canal. The glass fragments being on end, were demonstrated only on anteroposterior roentgenograms. A myelogram confirmed the presence of the glass in the sacral sac. Laminectomy was performed and the glass fragments were removed.

Glass is classified as of two main types: (1) "ordinary" glass, most often encountered as a foreign body, and (2) "lead" or "barium" glass. Ordinary glass is soda lime silicate, and is used for windows, mirrors, and bottles. It is of relatively low density and can be demonstrated in soft tissues of the extremities clear of bone, but not in thick areas such as the abdomen. Lead or barium glass, of higher density, is used in the base of light bulbs, fluoroscopic screens, and expensive crystal glass. When a glass foreign body is suspected and a similar fragment is available, the relative density of the glass can be determined by roentgenography of the sample. The literature shows little recording of glass as foreign body.

Three roentgenograms; 1 photograph.

J. S. ARAJ, M.D.  
Toledo, Ohio

**A Case of Robert's Pelvis.** Ethna W. Little. *J. Obst. & Gynaec. Brit. Emp.* 65: 465-471, June 1958. (Elsie Inglis and Bruntsfield Hospitals, Edinburgh, Scotland)

The symmetrical transversely contracted pelvis due to absence of both sacral alae, first reported by Robert in 1842, is by far the rarest type of deformed pelvis. Only 10 other cases have been recorded in the literature, and it is doubtful if all of these are indeed true Robert pelvises.

The author's patient was a 17-year-old girl. X-ray measurements of the pelvis in this case and of 2 dried specimens from the Manchester and Edinburgh University museums are compared with illustrations and measurements in Robert's original case. The Edin-



burgh pelvis is a virtual replica of Robert's case except that the transverse measurements are even smaller and there is an increase in the anteroposterior diameter of the outlet. The contour of the pelvis of the author's patient approximates Robert's case even more closely, but differs from it in that the sacroiliac synostosis, if present at all, is only unilateral and incomplete. The Manchester specimen exhibits certain recognizable differences. Rudimentary sacral alae are present, but from the roentgenograms the articular surface of the lateral mass appears to have extended upward on the iliac bone in an attempt to form an adequate sacroiliac synchondrosis, but evidently the surface area presented has been insufficient to allow normal stabilization of the pelvis and the support normally necessary to maintain the innominate bones in their correct position. As a result, the forces transmitted through the femurs have compressed the pelvis inferior to its reduced sacral support, while everting the ilia to some extent about this point, so that the shape and measurements at the brim are transitional between a normal and a Robert pelvis, while the outlet configuration is typical of a Robert pelvis.

At no time has any author disagreed with the conclusion that the Naegele and Robert pelvises are the unilateral and bilateral forms of the same condition. Study of the 4 cases in this paper reveals no evidence of previous osteitis. X-ray examination shows the bone texture to be quite normal, and in the pelvis with sacroiliac fusion, the trabeculae can be seen passing without interruption from the sacrum into the ilium, a feature noted by Williams when describing a Naegele pelvis in 1929 (*Am. J. Obst. & Gynec.* 18: 504, 1929). These findings support the theory of congenital absence of whole or parts of the centers of ossification of the sacral alae, to which the changes in the innominate bones are secondary. It is suggested that sacroiliac synostosis is an independent congenital anomaly which may occur unilaterally or bilaterally, alone, or in association with the Robert or Naegele pelvises.

The author believes that the term Robert pelvis should be reserved for the grossly transversely contracted pelvis due to congenital absence of the sacral alae, whether complete or partial.

Six roentgenograms; 1 photograph; 3 drawings; 3 tables.

**The Vessel Anatomy of the Upper Femur End with Special Regard to the Mechanism of Origin of Different Vascular Disorders.** Anders Hulth. *Acta orthop. scandinav.* 27: 192-209, 1958. (University of Uppsala, Uppsala, Sweden)

Several attempts have been made to develop a technique for the early diagnosis of avascularity of the femoral head in traumatic disorders. The author believes that intra-osseous venography yields more information than arteriography because of the small size of the arteries which are of special interest. Since the vessel supply of the head of the femur is characterized by parallel arteries and veins, it may be concluded from positive findings of typical head veins that the corresponding arteries also exist. For use particularly in the study of neck fractures, a tapered cannula of stainless steel has been made, provided with an obturator. The cannula is 10 cm. long, with an inner diameter of 2.3 mm., and has a handle for insertion and withdrawal. Two portable x-ray machines are employed and must be in position throughout the entire procedure.

Venography is performed no earlier than the third day after the fracture. The fracture is first reduced. The cannula is carefully positioned in the trochanteric fragment under roentgen control and then hammered, for a previously calculated number of centimeters, far into the head. Two milliliters of contrast medium (35-50 per cent Umbradil) is injected and an anteroposterior radiograph is obtained at the very end of the injection, followed by a lateral view immediately thereafter. Two minutes after the first exposure, a second anteroposterior radiograph is made. Before withdrawing the cannula, 1-2 ml. of physiological saline is introduced to wash out the remaining contrast material. Filling of the veins occurs instantaneously.

The author distinguishes between positive and negative venograms, the former with contrast-filled veins (circumflex veins or teres veins), the latter without visible veins. If the cannula has been placed correctly, i.e., far into the central part of the head and with no extra holes created, the negative venograms indicate avascular head fragments.

From his own findings and those of others, the author describes the vessel supply of the femoral head at different ages. Residual vascularity in different types of fractures (and in traumatic dislocation) is analyzed with the aid of the venographic method. In childhood according to Wolcott's (*Surg., Gynec. & Obst.* 77: 61, 1943. *Abst. in Radiology* 42: 204, 1944) and Trueta's (*J. Bone & Joint Surg.* 39-B: 358, 1957) investigations, the vessel supply of the epiphysis is very vulnerable because the epiphyseal plate constitutes a vascular barrier, and the only real supply of the epiphysis is a single group of vessels (the superior retinacular vessels). Nourishment via the ligamentum teres does not exist before the age of about eleven years. Intra-articular affections of different kinds may cause damage to the retinacular vessels, and disorders similar to Legg-Perthes' disease may occur. The vessel supply of the epiphysis in cases with slipped epiphysis is described, and the risk of damaging the vascular system with different methods of treatment is emphasized.

Eleven roentgenograms; 1 photomicrograph; 1 table.

**Tomographic Analysis of Depressed Fractures Within the Knee Joint, and of Injuries to the Cruciate Ligaments.** Stig Fagerberg. *Acta orthop. scandinav.* 27: 219-227, 1958. (Royal Academic Hospital, Uppsala, Sweden)

A series of nearly 200 cases of manifest or suspected fracture of the knee were examined by tomographic and standard x-ray technics. Both types of radiographs were taken in frontal and lateral projection, and standard radiographs also were obtained in one or two oblique projections.

Of 126 fractures, 8 were detectable only by means of tomography. All 8 involved the middle or posterior parts of the lateral tibial condyle; all consisted of a depression not exceeding 2 mm. in depth, without demonstrable compression of the underlying spongiosa.

In 12 cases in which standard radiographs indicated an injury by revealing a zone of compression in the spongiosa, it was possible to localize and accurately assess the lesion only with the aid of tomograms; in 8 of these cases the zone of compression was situated in the lateral tibial condyle or the anterior intercondylar fossa.

In the larger, depressed fractures, tomography regularly showed in greater detail the location and extent



of the injury, and in several cases was the deciding factor for or against operative reconstruction. The postoperative state of the joint could be judged in detail, a point of great importance after extensive structural alteration: the greater the divergence from the normal state due to arthrosis, sclerosis, osteoporosis, or deformity, the greater the need for tomography.

The demonstration of injury to the cruciate ligaments is important, both for treatment and prognosis. The ligaments are difficult to visualize by standard arthrography because of overlying structures and because of collections of contrast medium in the interior of the joint and in surrounding bursae and recesses. The assessment of injuries to the cruciate ligaments is limited by anatomical factors, but in every one of the cases in which it was employed, tomography helped to clarify the diagnosis.

The technic employed is as follows: Contrast medium is introduced into the joint by the method of Lindblom (*Acta radiol. suppl.* 74, 1948). Tomography is then carried out in lateral projection, with the knee flexed 45-90°. Four tomograms at 0.5-cm. intervals are usually enough to visualize the interior of the joint and clearly demonstrate the cruciate ligaments.

Twenty-two roentgenograms.

**The Ossification and Vascularisation of the Tarsal Navicular and Their Relation to Köhler's Disease.** W. Waugh. *J. Bone & Joint Surg.* 40-B: 765-777, November 1958. (54 The Ropewalk, Nottingham, England)

Normal and abnormal patterns of ossification and vascularization of the growing tarsal navicular and their relation to Köhler's disease were investigated in material consisting of (1) serial radiographs of 52 normal children's feet, (2) postmortem vascular injection studies, and (3) records of 62 children with Köhler's disease. The serial radiographs consisted of lateral projections of both feet taken at six-month intervals between the ages of two and five years inclusive. Study of these films showed that ossification occurs later in boys, abnormalities of ossification are more common in boys, and abnormalities are more frequent in naviculars that ossify late. Abnormalities of ossification may consist of only minor irregularities in shape or size, or gross changes indistinguishable from Köhler's disease.

Postmortem vascular injection of 21 naviculars revealed a dense perichondral network of vessels on the nonarticular surfaces, and from this numerous arteries penetrated toward the center of the cartilage. Ossification begins with bone formation in relation to a single artery and vein. Most commonly, other radial vessels become incorporated in the bony nucleus and form a dense anastomotic network. Less often, a single artery may be responsible for the nutrition of almost the whole nucleus. A third possible pattern is the development of several separate centers of ossification around several penetrating arteries, but no examples of this type were seen in the author's postmortem studies.

Forty-nine of the 62 patients with Köhler's disease were boys. The average age at onset of symptoms in boys was five years and one month, and in girls, three years and ten months. Two general types of radiological abnormalities were found in these cases. In the larger group, initial x-rays showed flattening of the navicular with patchy areas of increased density and loss of normal trabeculae. Early films in the second group showed the navicular to be of normal shape but

uniformly increased in density. During ensuing months, the dense bone was absorbed and only a faint narrow shadow remained. Approximately two years after onset, the navicular re-forms in both types.

The author proposes that abnormal ossification results from compression of the bony nucleus at a critical phase during growth of a navicular bone whose appearance is delayed. Further compression produces vascular changes in the bony nucleus and symptoms occur. The two radiographic types of Köhler's disease are attributed to variations in vascular supply, and the usual complete recovery of the navicular is probably due to the presence of numerous radially penetrating arteries.

Seventeen illustrations, including 13 roentgenograms.  
SAMUEL B. HAYESON, M.D.  
Lynwood, Calif.

### THE SPINAL CORD

**Arterial Anomalies of the Spinal Cord. Myelographic Diagnosis and Treatment by Section of Dentate Ligaments.** Paul Teng and Marvin J. Shapiro. *Arch. Neurol. & Psychiat.* 80: 577-586, November 1958. (130 N. La Cienega Blvd., Los Angeles 48, Calif.)

Arterial anomalies of the spinal cord are not too uncommon a cause of subjective and objective changes. The symptoms vary according to the level and severity of the anomaly. A picture of myelitis is present, with paraplegia and sensory and motor changes in the extremities or bladder. The changes may be intermittent or progressive. The diagnosis is made from myelographic studies which show rather typical linear or worm-like filling defects in the column of oil. This typical appearance, however, may be absent and disk-like defects or a block may be demonstrated. The condition, is nevertheless evident on surgical exploration.

The authors use 10 c.c. of Pantopaque and supplement the routine myelographic study by observation and films in the supine position, since most of the arterial anomalies are on the dorsal aspect of the cord.

Six cases are reported and 23 from the literature are reviewed. The combined series is tabulated as to level of lesion, its duration, myelographic findings, treatment, and results. In 5 of the authors' patients good results were obtained with laminectomy and section of the dentate ligaments. One patient treated by laminectomy alone showed no appreciable improvement. The role of the dentate ligament in producing symptoms and signs in degenerative conditions of the spinal cord is emphasized.

One photograph; 1 table.  
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Toledo, Ohio

### GYNECOLOGY AND OBSTETRICS

**Pelvic Angiography—With Particular Reference to Its Value in Intrauterine Pregnancy After the Fifth Month of Gestation.** K. E. Hodge. *Am. J. Roentgenol.* 80: 651-663, October 1958. (Sunnybrook Hospital, Toronto 12, Ontario Canada)

The author regards angiography as ancillary to plain film technic for locating the placenta and therefore uses it in few cases. After the thirty-second week of gestation 95 per cent accuracy of placental location is achieved with gravitational plain film technic. Cases in which placenta praevia is suspected earlier in

the course of pregnancy and occasional instances of abnormal presentation afford the chief indications for pelvic angiography. The author used it also in 2 patients with pelvic tumors associated with pregnancy.

The technic is summarized as follows: 1. Suitable premedication; no general anesthetic is required but local infiltration is used. 2. Rinsing of the arterial cannula, trocar, and guide wire in 1:1,000 heparin solution prior to the arterial puncture. 3. Percutaneous femoral puncture and retrograde cannulation of the ipsilateral external iliac artery as described. 4. Injection of 30 c.c. of 35 per cent Diodrast with a manual injector. 5. Exposure of two 14 × 17-inch films at three-second intervals. 6. Slow perfusion of the cannula with saline until the films are developed. 7. If the roentgenograms are satisfactory, the cannula is withdrawn and the site of percutaneous puncture manually compressed for five minutes.

Only one major complication arose in the author's 19 cases. Early in the series a small blood clot formed, entering a terminal branch of the right superficial epigastric artery and causing a local infarct with necrosis of the tissues of abdominal wall. The needle was not heparinized on that occasion.

Although the method employed has been of excellent assistance in the cases presented, its still questionable utilization by obstetricians raises doubt in the mind of the author concerning the real value of the procedure.

Nine roentgenograms; 1 photograph; 6 diagrams.

JOSEPH P. TOMSULA, M.D.  
Baton Rouge, La.

**Enlargement of the Placenta as Demonstrated by Soft Tissue Placentography.** James W. Ryel and George Jacobson. *Am. J. Roentgenol.* **80**: 639-650, October 1958. (1200 N. State St., Los Angeles 33, Calif.)

The technic of placentography used by the authors consists of roentgenography of the abdomen in the anteroposterior, right posterior oblique, left posterior oblique, and left lateral projections. A differential absorption filter is employed for the oblique and lateral views. It is estimated that radiation to the fetus is less than 2 r per exposure. Since these studies are done almost entirely on patients who are either actively bleeding or give a history of bleeding, and in view of the seriousness of the suspected diagnoses, it is not felt that this exposure is excessive.

The authors have found that the normal placenta may measure as much as 9 cm. in thickness. Only in cases with unequivocal findings is the diagnosis of an enlargement of the placenta made.

The authors' cases are divided into two groups: Group I, those with actual placental enlargement, and Group II, those with simulated placental enlargement. True enlargement is the result of erythroblastosis, premature separation, syphilis, diabetes, placental tumors, and continued growth of the placenta after fetal death. Erythroblastosis and premature separation are by far the most common causes. Pseudo-enlargement is attributable to polyhydramnios, abnormal presentation of the fetus, tumors or abnormalities of the uterus, abnormalities of the fetus, and prematurity.

Each of the above groups is individually discussed with case presentations.

Eighteen roentgenograms.

JOSEPH P. TOMSULA, M.D.  
Baton Rouge, La.

## THE GENITOURINARY SYSTEM

**Pyelographic Diagnosis of Lesions of the Renal Papillae and Calyces in Cases of Hematuria.** Benjamin S. Abeshouse and Julian O. Salik. *Am. J. Roentgenol.* **80**: 569-589, October 1958. (1714 E. Monument St., Baltimore 5, Md.)

This study merits careful consideration by all who have done, are doing, or will do urologic studies. Only the authors' tabulation of lesions of concern is presented here to show the scope of the work.

### *Diseases of the Renal Papillae and Calyces*

#### I. *Inflammatory hyperplastic lesions*

1. Nonspecific granuloma
2. Specific granuloma
3. Proliferative solitary polypoid hyperplastic granuloma
4. Pyelitis cystica; pyelitis granulosa
5. Localized hyperplastic cystic formation.

#### II. *Metaplastic lesions*

1. Foam-cell granuloma

#### III. *Nonspecific infections*

1. Pyelonephritis, acute, chronic and focal
2. Hemorrhagic papillitis
3. Necrotizing papillitis
4. Abscess of the kidney

#### IV. *Specific infections*

1. Tuberculosis; tuberculoma
2. Syphilis; gumma

#### V. *Cystic lesions*

1. Serous cyst, superficial and deep
2. Papillary cyst
3. Pyelogenic cyst
4. Calyceal diverticulum
5. Hydrocalyx
6. Multiple cysts of pyramids; "sponge" kidney
7. Peripelvic cyst
8. Echinococcus cyst
9. Polycystic disease, unilateral and bilateral

#### VI. *Benign tumors*

1. Adenoma
2. Lipoma; replacement lipomatosis
3. Fibroma
4. Hamartoma

#### VII. *Malignant tumors*

1. Tubular origin—adenocarcinoma, hypernephroma
2. Epithelial origin—squamous-cell carcinoma, papillary carcinoma of the pyelocalyceal system

#### VIII. *Vascular tumors*

1. Benign—varix, angioma
2. Malignant—hemangiosarcoma, etc.

#### IX. *Miscellaneous lesions*

1. Nonradiable calculi
2. Crystalloid infarction or infiltration of papillae
3. Renal infarction and embolism
4. Leukoplakia
5. Malacoplakia
6. Papillary infiltration by hemopoietic disease
7. Papillary involvement by metastatic tumors

8. Endometriosis
9. Actinomycosis
10. Perirenal hematoma or abscess

Each of these lesions is discussed from a pathologic standpoint. The outstanding urographic changes are described, and representative pyelograms are reproduced. The authors hope that knowledge of the type presented will eliminate most of the diagnostic uncertainty in the group of obscure cases of renal hematuria so commonly classified as idiopathic.

Sixty-two roentgenograms.

JOSEPH P. TOMSULA, M.D.  
Baton Rouge, La.

**Nephrocalcinosis: A Roentgenologic, Biophysical and Histologic Study.** Bengt Engfeldt and Curt Lagergren. *Acta chir. scandinav.* 115: 46-57, 1958. (University of Uppsala, Uppsala, Sweden)

In an investigation of nephrocalcinosis, the deposition of mineral salt in the renal parenchyma was studied in kidneys from 103 consecutive routine autopsies. Standard roentgenography, microradiography, roentgen crystallography and microscopy were employed. In 26 cases (25 per cent) the kidneys showed calcifications exceeding 0.1 mm. in diameter. Crystallographic analysis revealed only three substances—the two calcium oxalates and basic calcium phosphate. Some of the microliths had the same crystallographic and morphologic structure as fully developed oxalate stones. One interesting finding was the presence of small intratubular casts of calcium salt in all 26 cases with roentgenographically observed calcifications. The casts were all of similar appearance and seemed to be composed of basic calcium phosphate. The association between these deposits and the development of urinary calculi is discussed.

Two roentgenograms; 10 microradiograms; 1 table.

**The Use of Miniature Film (Renogram) for Kidney Stone Surgery.** C. R. Marquardt, J. W. Pick, A. Melamed, A. Marck, and A. H. Holt. *J. Urol.* 80: 388-392, November 1958. (Deaconess Hospital, Milwaukee, Wisc.)

In order to insure the complete removal of multiple kidney stones and fragments of stones a film taken during operation is imperative.

The authors advocate the use of a miniature film enclosed in an inexpensive, disposable, plastic cassette  $1/16$  inch thick. The cassette is notched to identify accurate placement at the renal hilus and wedged to identify the outer upper pole. The film is removed from the cassette by cutting along the outer surface and sliding it out without causing any crease marks that might interfere with interpretation. Routine development is adequate.

This film has proved a valuable aid in operative roentgenography, and it is believed that it will materially lessen the incidence of pseudo-recurrences.

Twenty-two roentgenograms; 1 photograph; 1 table.

SAUL SCHEFF, M.D.  
Boston, Mass.

**Metastatic Malignant Melanoma of the Kidney Simulating a Primary Neoplasm. A Case Report.** Colvin H. Agnew. *Am. J. Roentgenol.* 80: 813-816, November 1958. (University of Texas Medical Branch, Galveston, Texas)

A 57-year-old male complained of intermittent urinary

bleeding of six months duration but no other urinary difficulties. He gave a history of iridectomy in 1941 and a diagnosis of diabetes mellitus established in 1927. Physical and laboratory findings were not specifically important. Retrograde pyelography demonstrated a mass in the upper pole of the left kidney with blockage of the adjacent renal pelvis and calyces, suggesting a diagnosis of renal-cell carcinoma. Excretory pyelography, however, showed no destructive lesion of the left kidney but a mass obstructing the renal pelvis. Consequently, the preoperative diagnosis was changed to tumor of the renal pelvis. At surgery the kidney was readily removed. Section showed a reddish black mass in the renal pelvis about 2.5 cm. in diameter, slightly adherent to the pelvic epithelium, presenting the gross appearance of a partially organized blood clot. Microscopic sections resulted in a diagnosis of melanoma. A similar, small, bean-shaped mass found in the omentum subsequently proved to be a similar tumor lesion. No information on the patient's subsequent course is given.

Gross metastatic deposits in the kidneys are relatively rare; they are usually located in the renal cortex, are commonly associated with widespread terminal disease, and are seldom a cause of symptoms. The case reported is considered of interest because of its failure to accord with these concepts. It is felt by the author that the most likely site of the primary tumor was the diseased eye, although this was never proved.

Previously published information is cited to explain possible modes of renal pelvis implantation. The interesting possibility of excretion of the intact tumor cell by the renal tubules followed by implantation in the renal pelvis is proposed. Some theories as to why certain organs are victims of metastases while others appear relatively immune are discussed.

Two roentgenograms; 3 photomicrographs.

JAMES W. BARBER, M.D.  
Cheyenne, Wyo.

**A Case of Sponge Kidney.** G. Reboul, M. Pélissier, and L. Beltrando. *J. de radiol.* 39: 795-796, November 1958. (In French)

A rather uncommon condition consisting of congenital development of cysts around multiple calyces of the kidneys has been called "sponge kidney" or "spongy kidney." The case reported here occurred in a 49-year-old man who had had intermittent hematuria for several years. There was no pain, nor were albumin, pus, or bacteria found in the urine. Intravenous urography demonstrated a series of small, irregular cyst-like cavities branching around the calyces like "bouquets of flowers."

This condition is usually bilaterally symmetrical, but may occasionally affect only one kidney. Approximately half of the cases will have multiple calcifications in the small cyst-like spaces about the calyces, leading to confusion with nephrolithiasis.

One roentgenogram.

CHARLES M. NICE, JR., M.D., Ph.D.  
Tulane University

**A Classification of the Urographic Patterns in Children with Congenital Bladder Neck Obstruction.** Aurelio C. Uson, Donald W. Johnson, John K. Latimer, and Meyer M. Melicow. *Am. J. Roentgenol.* 80: 590-602, October 1958. (620 W. 168th St., New York 32, N. Y.)

Since children with congenital bladder neck obstruction

tion usually appear healthy and well nourished when first seen, despite the fact that their urinary tracts may be seriously affected, the authors have formulated a classification which would be an aid in the initial evaluation of these patients. This serves also as a guide to treatment and determination of its effectiveness.

The classification was derived from a study of cystograms, urograms, and retrograde pyelograms of 158 children (100 boys and 58 girls) seen between 1938 and 1957. The cases are divided into two groups, based upon the presence or absence of vesico-ureteral reflux. Each group is further subdivided into three types according to the status of the upper urinary tract. An excellent pathologic and physiologic discussion of each group and subtype is given, and cases documented by radiographs and sketches are concisely reported. Additionally, a theory as to the genesis of the juxta-meatal vesical diverticula is offered.

Twenty-two roentgenograms; 4 photographs; 2 groups of multidiagrams.

JOSEPH P. TOMSULA, M.D.  
Baton Rouge, La.

**Spontaneous Extravasation During Urography.** William E. Forsythe, William L. Huffman, Paul J. Schildt, and Lester Persky. *J. Urol.* 80: 393-398, November 1958. (900 Keith Bldg., Cleveland 15, Ohio)

The authors report the case histories of 7 patients in whom extravasation of the contrast medium from the urinary tract during excretory urography could not be explained by backflow into commonly recognized channels. Such extravasation, the authors believe, may represent "not so much an escape . . . from the renal pelvis as an escape from the lymphatics whose capacity has been exceeded during backflow phenomena."

The first 3 patients all presented with signs or symptoms referable to the left flank. In all 3 there was extravasation of contrast medium apparent as a wide opaque band of density along the upper and middle third of the psoas shadow, distinct from the collecting system. On re-examination there was no repetition of the extravasation; in the case explored no site of rupture was found to explain the presumed leak.

The fourth case of extravasation occurred in a patient following panhysterectomy. Uretero-neocystostomy was ultimately performed, with relief of all symptoms. A fifth case followed pelvic surgery, with kinking of the ureter; removal of the kinking suture led to recovery. In another patient with a left ureteral stone there was extravasation from the right kidney, which yielded turbid urine on perinephric exploration. The stone was extracted and subsequent urograms were normal. In the last case the preoperative diagnosis was appendicitis but laparotomy revealed a free collection of periureteral urine, which was drained with a T-tube, although no rent in the ureter could be identified.

The recognition of the roentgenographic picture as indicative of an essentially benign, transitory process in most cases may prevent hasty surgery.

Ten roentgenograms.  
SAUL SCHEFF, M.D.  
Boston, Mass.

**Views on the Value of Urethrocytography in Determining Indications for Surgery in Prostatic Hypertrophy.** Hans Ekman. *Acta chir. scandinav.* 115: 18-24, 1958. (Sahlgrenska Sjukhuset, Gothenburg, Sweden)

In many hospitals urethrocytography is now carried

out routinely in the patient with hypertrophy of the prostate it having been felt that a hypertrophic gland should preferably be operated upon before the condition has progressed far enough to produce dilatation of the ureters and renal pelvis, with subsequent impairment of renal function.

The author made a study of 370 cases treated by transvesical or retropubic prostatectomy. Three hundred and fifty-nine of the men had preoperative urograms. In no case did these studies corroborate the theory that dilatation begins in that part of the ureter crossed by the vas deferens. The preoperative urograms not infrequently showed the dilated ureters to become narrowed and compressed as they entered the bladder wall. At this point the bladder wall sometimes displayed a crescent-shaped impression of the lower part of the ureter. In the author's opinion, therefore, the cause of ureteral and renal pelvic dilatation in prostatic hypertrophy, particularly in the early stages, is an altered condition of the bladder wall.

The association between pathological changes in the bladder wall and ureteral dilatation was studied in 188 cases in which preoperative urography and urethrocytography were done. Of the 25 patients with the most severe bladder changes—trabeculation and diverticula—no less than 16 (64 per cent) had dilatation of the upper urinary tract. Of the 127 men with less pronounced trabeculation, 14 (11 per cent) showed such dilatation. Eleven of the 18 men with dilatation of the renal pelvis and ureters had severe bladder trabeculation, while the other 7 had milder changes of this type.

Three of the 30 patients with dilatation of the upper urinary tract and bladder lesions had less than 100 ml. of residual urine.

The author concludes that bladder wall changes constitute one of the surest and most objective signs of difficulty in bladder emptying associated with prostatic hypertrophy. Preoperative urethrocytography or cystoscopy must therefore be ascribed particular importance in diagnostic investigation and in assessing the indications for surgical intervention.

Eight roentgenograms; 1 table.

#### TECHNIC; NOMENCLATURE

**Quantitative Aspects of Television Techniques in Diagnostic Radiology.** G. A. Hay. *Brit. J. Radiol.* 31: 611-618, November 1958. (Department of Medical Physics, University of Leeds, England)

The author deals with the inefficiencies of image production by conventional methods of radiography, fluoroscopy, and cinefluorography in considerable detail. Newer methods of image intensification utilizing image converter tubes and solid screen electron multiplication are considered and their deficiencies pointed out.

A careful analysis of the desirable qualities of an ideal image detector is presented. The author feels that these requirements might best be met with an application of television scanning technics. The gain of such a system is derived mainly from thermionic valve circuits and in practice is limited only by fluctuations introduced by the valves themselves or by other components. The output of the system forms an image on a cathode-ray tube, as in the familiar television receiver; thus the brightness level can be high, the screen is relatively easy to photograph, and many receivers may be used at almost any desired distance from the



patient. Because the output is in electrical form, it may be stored in an electronic storage tube or recorded more permanently on magnetic material. Finally, the contrast of the image may be varied electronically, and backgrounds such as scatter may be subtracted by similar means.

Such an image detection system is in use at Leeds General Infirmary, and experience with it since 1957 is described. Image resolution is somewhat limited, and the equipment is bulky and rather inflexible, but it is believed that improved television camera tube design will overcome some of the present inadequacies.

Five roentgenograms; 1 photograph; 1 chart; 2 tables.

MAJ. BYRON G. BROGDON, M.C.  
Lackland AFB, Texas

**Television Pick-Up Tubes for X-Ray Screen Intensification.** G. B. Banks. *Brit. J. Radiol.* 31: 619-625, November 1958. (English Electric Valve Co. Ltd., Chelmsford, Essex, England)

The two principal advantages of screen intensification are: (1) elimination of dark-adaptation, thereby improving the visual resolution of the operator, and (2) diminution of radiation to patient and operator.

Several workers have utilized devices developed for television in an attempt to achieve the ideal x-ray intensifier. A detailed description of the television pick-up tube (image orthicon) is presented and deficiencies of the standard 3-inch tube commonly used are analyzed.

The author has developed an improved pick-up tube which is fully described and diagrammed. It apparently offers a number of advantages over the standard image orthicon, in the laboratory, being more efficient. Clinical tests had not yet been undertaken.

Six figures. MAJ. BYRON G. BROGDON, M.C.  
Lackland AFB, Texas

**Pelvic Lymphography.** P. Leenhardt, R. Colin, and H. Pourquier. *J. de radiol.* 39: 778-781, November 1958. (In French) (Centre anticancéreux de Montpellier, France)

The authors describe their technic for demonstration

of the pelvic lymphatics. After premedication followed by local anesthesia, an incision of 3 to 4 cm. is made in the region of the femoral vein just below the inguinal ligament. The small lymphatics are found near the vein at the upper border of the pectineus muscle. After one of the small lymphatics is cannulated from 2 to 10 ml. of a 70 per cent water-soluble contrast agent is injected. Films of the pelvic region are then taken, showing the lymphatics which may be displaced by benign tumors or blocked by malignant tumors of various types.

Seven roentgenograms.

CHARLES M. NICE, JR., M.D., Ph.D.  
Tulane University

**"Flat Film" of the Abdomen.** Harry L. Arnold, Jr., and P. J. Washko. *J.A.M.A.* 167: 773-774, June 7, 1958. (1020 Kapiolani St., Honolulu, Hawaii)

The time-honored expression "flat film" of the abdomen is an unpopular one among radiologists generally. It deserves, according to the author, to be more unpopular than it is, because there is no general agreement as to its meaning.

Sixteen American radiologists were asked to define the term "flat film." A film obtained in the horizontal position received 10 votes, with "no contrast medium" 7 votes, and "not stereo" 6 votes, a total of 23 meanings divided among 16 men, of whom 12 chose only one of the three possible meanings, and only 2 chose all three. It seems clear from this that it would be difficult, if not impossible, to secure general agreement on the meaning of the expression "flat film of the abdomen." It is hopelessly ambiguous and should really be abandoned.

Thirteen of the 16 radiologists queried suggested other terms. "Scout film" was recommended by 7 and "plain film" by 3. Other terms were "preliminary film," "KUB," "survey," "exploratory" or "AP or PA." Either "scout film" or "plain film" of the abdomen would generally be understood to mean a single (nonstereoscopic) roentgenogram in an unprepared patient. To either of these phrases should be added a qualifying designation of position: supine (for posterior structures, equivalent to the "KUB"), prone (for the anterior abdomen), upright, or lateral.

## RADIOTHERAPY

**Discussion on Pituitary Tumours.** Harvey Jackson, J. Jackson Richmond, and S. Leonard Simpson. *Proc. Roy. Soc. Med.* 51: 907-916, November 1958. (London, England)

In this discussion on pituitary tumors, the subject of radiotherapy is considered by Richmond. Jackson, who introduces the symposium, deals chiefly with the general features of pituitary growths. He mentions treatment by irradiation but does not favor its use, pointing out that cystic tumors do not respond to irradiation; that Rathke pouch tumors are not favorably influenced by high-voltage therapy; that in large series the response has been unsatisfactory in more than 50 per cent of cases; that high-voltage therapy may have disastrous effects.

Richmond refers to the increasing use of irradiation for tumors of the pituitary and considers the advantages of combined surgery and radiotherapy. Preliminary surgical exploration and partial excision of an adenoma permit (1) immediate decompression of the visual pathways; (2) direct assessment of the size and extent of the

tumor; (3) histological verification. Operative mortality in skilled hands is said to be low.

Review is made of 220 cases treated by irradiation. More than two-thirds of these were chromophobe adenomas and the rest were approximately evenly divided between eosinophilic tumors, basophilic tumors, craniopharyngiomas, and carcinomas [metastatic?]. In the chromophobe adenoma group 87 per cent of the radiologically treated cases showed some form of visual improvement, very marked improvement in one-third and moderate in two-thirds. Eight of 9 patients with basophilic lesions displayed some degree of improvement. Evaluation of endocrine changes in chromophobe or eosinophilic tumors following therapy is more difficult to assess. The author notes that the response of craniopharyngiomas to irradiation is decidedly encouraging in some cases.

A summary of results as expressed in survival rates shows five-year survival between 75 and 90 per cent for the commoner tumor types. The carcinomas showed only 57 per cent five-year survivals. Investigation of



patients dying of their tumors revealed the cause of death most commonly to be intracranial extension of recurrent adenoma or extreme hypopituitarism.

A brief comment on radiotherapeutic technic indicates use of conventional x-ray modalities (3 mm. Cu h.v.l.). The author uses five small square fields 4 cm. on a side, carefully aimed at the pituitary by means of a beam-directing jig. Dosage to the sella is 3,750 r (maximum) in four weeks.

The endocrine aspects of this group of tumors is taken up by Simpson. Chromophobe tumors are frequently unrecognized for several years as the patient goes through various subclinical endocrine disturbances with gradual progression to frank clinical manifestations, usually of pituitary hypofunction. The point is made that advanced endocrine deficiencies or abnormalities may be present in the absence of prominent visual changes. A single lateral skull roentgenogram will frequently permit diagnosis. In acromegaly, the diagnosis likewise may be delayed for many years. A discussion of substitution endocrine therapy is given. Seven roentgenograms; 3 tables.

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**Results of Roentgen Treatment of Acromegaly. A Clinical Review.** Bengt Arner, Martin Lindgren, and Bengt Lindqvist. *Acta endocrinol.* 29: 575-586, December 1958. (University Hospital, Lund, Sweden)

Since the course of acromegaly is unpredictable, caution must be exercised in the evaluation of the results of therapy in a given case. The principles of treatment established around 1920 have undergone no significant modification. It is generally considered that all patients with symptoms of compression of the optic nerve should be treated surgically. Most neurosurgeons, however, regard patients with acromegaly as poor risks because of the danger of hemorrhage in the operative field. During the years 1946-55, only 4 patients were operated on in the Department of Neurosurgery, University Hospital, Lund, because of optic nerve compression. In the absence of pressure symptoms, treatment usually consists of roentgen irradiation of the hypophysis.

Between 1922 and 1953, 20 patients with acromegaly received roentgen therapy only, and in 1954-55 the authors carried out an investigation of the 16 survivors. The examination was fairly complete from a medical and endocrinological point of view. The average age of the 16 patients at the time of follow-up was fifty-one years. The average interval since treatment was twelve years; 10 patients had survived for nine years or more. Severe or moderate changes of acromegaly were present in 10 of the 16 surviving patients; in none was any progression of the disease apparent. A certain improvement was noted, due mainly to abatement of the swelling of the soft tissues. Most of the patients stated, without being asked, that the hands and fingers had become thinner and more flexible and that numbness of the hands and feet had disappeared after roentgen therapy. No regression in the acromegalic growth disorders had occurred. There was no evidence of development of adrenocortical insufficiency following irradiation.

Hypertension and cardiovascular disease are considered a serious complication of acromegaly; there was no excessive morbidity from cardiovascular disease in

the present series. The sella turcica was more or less severely enlarged in as many as 75 per cent of the patients at the beginning of roentgen therapy. In 15 of the 16 patients living at the time of the review, the size was unaltered. In 1 patient there was a somewhat increased downward excavation. One patient had a large visual field which was considerably diminished by irradiation. In none of the patients had pressure symptoms appeared.

The roentgen doses delivered varied during the thirty-year-period under consideration. On the basis of the authors' experience, a tumor dose of about 3,200 r in twenty days seems to be suitable. With shortening or lengthening of the treatment period, this dose must be decreased or increased because of the importance of the time factor in the recovery of tissues after irradiation. No serious reactions of the skin, skull, or brain were observed. As a rule, the skin showed only transient epilation and slight pigmentation.

It is concluded that roentgen therapy to the hypophysis in patients with acromegaly appears to be valuable in that it brings the growth disturbance to a standstill and sometimes produces a certain regression of the soft-tissue changes. The mortality and morbidity from cardiovascular disease are not high, and no severe symptoms of hypopituitarism develop.

**Cancer of the Breast. A Study of Short Survival in Early Cases and of Long Survival in Advanced Cases.** D. W. Smithers. *Am. J. Roentgenol.* 80: 740-758, November 1958. (Radiotherapy Department, Royal Marsden Hospital, London, S. W. 3, England)

The results of surgical and radiation treatment in breast cancer of Stages I and II have shown little improvement recently, indicating that the local therapeutic measures approach the optimum. Even so, these methods fail to deal with blood-stream dissemination. Various combinations of radiation and surgery may achieve equal cure rates, but are also equally ineffective in dealing with blood-borne metastasis. Radical operations are unjustified except in patients with extensive lymphatic spread and without hematogenous spread, but as yet clinical isolation of such cases is not feasible. Even if blood-stream dissemination can be excluded, extensive surgery is not necessarily the most effective treatment, since these patients may respond quite well to irradiation. Several factors should influence the type of treatment. These include the grade and size of the tumor, the length of the history, the site of the tumor, the age of the patient, and the probability of lymph node involvement. Two patients with breast cancer of the same stage may still present totally different clinical pictures, so that no rigid treatment plans are valid.

The grading of the tumor seems to be the greatest influence upon the ultimate outcome. Patients with Stage I, Grade I tumors who die of their disease have often been mismanaged, while patients with Stage I, Grade III tumors show few survivors even with proper management. There is a direct correlation of tumor grading and the incidence of axillary lymph node involvement.

The size of the primary tumor is also related to prognosis, and survival varies with the length of the history. In Grades I and II, in patients with a shorter history survival is greater; but in Grade III, the length of the history has little effect on the prognosis.

*Tumor site* is important prognostically. Inner quadrant lesions have a poorer prognosis than outer quadrant lesions owing to the involvement of parasternal lymph nodes. Consequently, a larger proportion of these patients are included in Stage I, when actually lymph node metastases exist that are not clinically detectable.

The *age of the patient* influences the prognosis but probably not as a result of the biological behavior of the tumor but because older women tend to wait longer before coming to treatment and, therefore, show a later stage distribution; and the treatments may be compromised and less energetic because of their age. These women are also subject to death from intercurrent disease, so that older patients in any given group of cancer of the breast will influence the survival statistics.

At Royal Marsden Hospital (London), 7 per cent of 583 patients with Stage I cancer of the breast died within two years of treatment. An analysis of these cases would indicate the influences on survival of grading, tumor-site, and other factors described above. All of these patients died of hematogenous metastases. Any more radical operative treatment, therefore, would not have been justified and, in fact, may have been contraindicated, since such procedures may hasten dissemination of the tumor.

In analyzing the advanced cases of breast carcinoma, it was obvious that the chance of cure is small regardless of the type of treatment employed. However, contrary to unimproved results in treating early stages, there has been improvement in the survival of the late-stage cases. The survival was still shown to depend upon the grade, size, and site of the lesion, and length of history. A study of 293 Stage IV breast cancer patients showed a survival of three years or more in 21. The length of survival varied up to thirteen years.

These studies permit the following conclusions: (1) Failure in early cases is usually due to distant hematogenous metastases. (2) Mastectomy is the treatment of choice in early cases, but points favoring a poor prognosis should limit, not extend, surgery. (3) Medial tumors with a short history justify preoperative irradiation, and all patients with medial quadrant tumors and all with outer half tumors with histologic involvement of axillary nodes should have postoperative irradiation to the axillary, supraclavicular, and parasternal lymph nodes. (4) Premenopausal patients having multicentric tumors, high-grade tumors, or extensive tumor permeation should be treated initially by induction of an artificial menopause. (5) In postmenopausal elderly patients, estrogen therapy should be combined with irradiation. (6) The more drastic therapeutic approaches of adrenalectomy and hypophysectomy should be reserved until the value of the accepted modes of therapy can be assessed in each patient.

Two roentgenograms; 3 photographs; 16 graphs; 7 tables.

JOHN W. WILSON, M.D.  
Johnstown, Penna.

**Radiation Therapy of Carcinoma of the Pancreas. Report on 91 Cases.** Theodore R. Miller and Lillian M. Fuller. *Am. J. Roentgenol.* 80: 787-792, November 1958. (Pack Medical Group, 139 E. 36th St., New York 16, N. Y.)

Carcinoma of the pancreas is usually recognized only in its advanced stages and is seldom cured by any form of therapy. Consequently, surgical measures are fre-

quently limited to endeavors to relieve jaundice or pain. Reports of average survival after such procedures vary from six to ten months.

This paper presents results of radiotherapy in 91 patients with advanced carcinoma of the pancreas which was explored, biopsied, and considered inoperable. Thirty-four patients were treated with 180 to 250-kv. x-rays, 12 with a 4-gm. telerradium pack, 20 with 1,000-kv. apparatus, and 20 with the 22.5-million-volt betatron. Interstitial radon seeds were used in 4 cases and 1 patient was treated with iridium 192. Radioactive gold, phosphorus, and chromic phosphate were employed in some instances to control ascites.

The best palliative results were obtained in patients with disease still fairly well localized to the pancreas and regional nodes and when irradiation was administered in the immediate postoperative period. A control group of 118 cases showed an average survival time of 6.1 months. The irradiated group as a whole had an average survival of 6.6 months after irradiation was begun. Twenty-nine per cent showed subjective improvement lasting from two weeks to two years, and 10 per cent were considered to have excellent results in respect to survival time and general condition. Jaundice and pain were often decreased or relieved so that the authors feel that some degree of palliation was achieved even when the survival time was not significantly altered. The authors point out that their experience would not substantiate the impression that radiation to the upper abdomen produces extreme radiation sickness and do not feel that this is a contraindication to radiation therapy for palliation in carcinoma of the pancreas. Persistent vomiting prior to any irradiation may constitute a contraindication to this type of therapy, however. The best results in this series were obtained with the 1,000 kv. roentgen-ray apparatus.

The following method of treatment is proposed: (1) exploratory laparotomy and biopsy if the patient is considered inoperable; (2) cholecystojejunostomy and gastroenterostomy in the presence of jaundice and duodenal obstruction; (3) implantation of radon or iridium 192 seeds; (4) subsequent external irradiation with a supervoltage apparatus in the 1-Mev range.

JOHN W. WILSON, M.D.  
Johnstown, Penna.

**Roentgen Treatment of Granulosa Cell Carcinoma of the Ovary.** Robert Bray Engle. *Am. J. Roentgenol.* 80: 793-798, November 1958. (St. Luke Hospital, Pasadena, Calif.)

Contrary to the common belief that granulosa-cell tumors of the ovary occur in adolescence, it has been shown that the majority appear in the postmenopausal age group. The tumors are usually unilateral and are frequently encapsulated, but occasionally show invasion and even distant metastases. Typically, a granulosa-cell carcinoma of the ovary manifests itself by the effects of hyperestrinism—precocious sexual development in adolescents, amenorrhea alternating with heavy flow in the child-bearing age, and vaginal bleeding and endometrial hyperplasia in the postmenopausal age. The mortality is approximately 25 per cent in patients with unilateral disease.

Primarily the treatment of granulosa-cell carcinoma of the ovary is surgical, and it is recommended that bilateral salpingo-oophorectomy and total hysterectomy be performed. Twelve cases are reported in which

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postoperative irradiation was given. In this group there were 4 long-term survivals (twelve to eighteen years) and 2 three-year survivals. All of these patients had extensive malignant involvement so that the survival is attributed to radiation therapy. Irradiation was usually initiated two to four weeks postoperatively, 1,800 r (air) being delivered to each of four pelvic ports.

Although there is disagreement in regard to the radiosensitivity of granulosa-cell tumors of the ovary, a definite radioresponse has been reported by several authors, and the experience with the 12 cases recorded here illustrates the efficacy of radiation in the treatment of this disease. Routine postoperative irradiation is recommended.

One table.

JOHN W. WILSON, M.D.  
Johnstown, Penna.

**Ewing's Sarcoma: Ten-Year Survivals. Report of a Case with Recurrent Pulmonary Metastases.** Harold N. Harrison. *Ann. Surg.* 148: 783-789, November 1958.

A case of Ewing's sarcoma with ten-year survival is reported. The patient was a 23-year-old male whose primary tumor was in the tibia, followed by two episodes of metastasis to the lung. The primary tumor was treated by high thigh amputation. The first metastasis in the lung was treated by surgical excision and the second by irradiation. At the time of the report the patient was clinically and roentgenographically free of recurrent or metastatic disease two and a half years after the last episode.

This is believed to be the only case recorded in the English literature of Ewing's sarcoma with pulmonary metastases which were treated surgically. It is also the first example of Ewing's sarcoma with recurrent pulmonary metastases and survival for ten years.

A review of the English literature reveals 19 cases of histologically proved Ewing's sarcoma, with survival of ten years or more, but no special features could be recognized which characterized this group prognostically. The five-year survival for this tumor varies from 4 to 10 per cent and no difference exists between surgery and irradiation or a combination of both, as a means of primary therapy.

Three roentgenograms; 3 photomicrographs; 2 tables.

RAUF YAGAN, M.D.

Cleveland Metropolitan General Hospital

**Roentgen Therapy in Hand-Schüller-Christian and Related Diseases.** Bertel Jørgsholm. *Acta radiol.* 50: 468-476, November 1958. (Radium Centre, Copenhagen, Denmark)

Hand-Schüller-Christian disease, Letterer-Siwe's disease, and eosinophilic granuloma of bone are considered to be manifestations of different phases of the same disease process. Letterer-Siwe's disease usually occurs at a somewhat earlier age than Hand-Schüller-Christian disease, of which it is believed by some to be an initial stage. Eosinophilic granuloma affects somewhat older children or even adults.

Fourteen patients suffering from those disorders have received roentgen therapy at the Radium Centre, Copenhagen, since 1933. Ten cases were diagnosed clinically as Hand-Schüller-Christian disease; 2 as Letterer-Siwe's disease; and 2 as eosinophilic granuloma. The ages of the patients varied from one to eight years.

The time observation ranged from one to twenty years. There was only 1 fatality. The cases followed a rather uniform pattern, with partial spontaneous remission as the usual outcome. The skeletal, cutaneous, pulmonary, lymphatic, and ocular manifestations regressed. Four patients at the time of the report still had diabetes insipidus and 2 patients were feeble-minded.

The treatment of these diseases is roentgenologic, except for solitary eosinophilic granulomas, which can be treated surgically. The skeletal lesions often disappear or regress following roentgen therapy. However, the role of irradiation in inducing these changes is difficult to evaluate, because spontaneous remission may have occurred.

Cautious, small fractionated doses of radiation are recommended. In the present series single doses to one field usually ranged from 5 to 100 r (air); total dose to each field 50 to 600 r (air). Rarely did a single field receive more than 1,000 r (air). Two patients in this series were treated with large doses to the skull lesions—3,675 and 10,000 r (air). Both of these patients were mentally retarded and were later declared feeble-minded.

The ultimate prognosis in these cases is governed generally by the age of onset and the course of the disease. The younger the patient at the onset, the more serious the prognosis. The course may vary from an acute, fulminating fatal disease to a chronic, quiet variety persisting for years.

Three roentgenograms; 1 table.

CAPT. ALLAN E. GREEN, JR., M.C.  
Lackland AFB, Texas

**Various Practical Methods of Grid Therapy.** Gerhart Baum. *Strahlentherapie* 107: 397-403, November 1958. (In German) (Städt. Krankenhaus München r. d. Isar, Germany)

Grid therapy was first described in 1909 by Alban Köhler, who hoped by this method to protect the skin and obtain a more homogeneous distribution of radiation at the site to be treated. The present author recommends a grid with openings of 1 cm. diameter and a ratio of 40 to 60 between the open and the covered areas. Daily dosages should not be higher than 500 r per field. The average total dose is 15,000 r, the highest being 23,000 r. For skin protection talcum powder and antihistamine ointments are advised.

In cases where, due to irregularity of the skin surface, the fields are somewhat overlapping and become confluent, no permanent damages have been observed.

The radiation of the uncovered areas may be as high as 20 per cent including back-scatter. It is therefore important to determine the maximum dose by calculating the total dose of the open and the uncovered fields. The total skin dose in grid therapy is approximately five times as high as in conventional roentgen therapy with stationary fields.

Grid therapy with multiple portals is of great value in the treatment of cancer of the lung and esophagus. If the tumor dose is over 6,000 r, the average survival of patients is doubled as compared with conventional methods. From clinical experience the author warns of single dosages higher than 500 r because of the danger of too rapid regression and necrosis of the tumor followed by severe hemorrhage.

Two photographs.

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## RADIOISOTOPES

**Positron-Scanning with Copper-64 in the Diagnosis of Intracranial Lesions: Partition of Copper-64 Versenate in, and Excretion from, the Body.** H. J. Bagnall, P. Benda, G. L. Brownell, and W. H. Sweet. *J. Neurosurg.* 15: 411-426, July 1958. (Harvard Medical School, Boston, Mass.)

The technic used and the results obtained with copper 64 in the localization of intracranial lesions are described and compared with those following the use of arsenic 74. The experimentally determined distribution and excretion of copper 64 both in normal and neoplastic tissues constitute the basis of this report.

The great majority of the patients studied received copper 64 as a versenate—copper-64-ethylene-diaminetetra-acetic acid (EDTA). The half-life of copper 64 is 12.8 hours; it decays, emitting gamma radiation of 1.34 Mev, with 19 per cent  $B^+$  emission, 42 per cent K-capture, and 39 per cent  $B^-$  emission. The dosage was 2.0 mc per 70 kg. body weight. Automatic coincidence scanning was used.

The copper-64 content was determined in three groups of specimens: (a) Plasma and erythrocyte concentration was determined in 4 and urinary excretion in 5 normal patients; (b) Biopsy samples of 19 areas of normal brain, 18 biopsies from patients with proved brain tumors, 14 biopsies of muscle, and 13 skull biopsies were also analyzed to determine differences in isotopic uptake in these tissues; (c) Autopsy material in 1 case provided data on copper-64 concentration in the major organs and tissues of the body.

It was found that within two hours of injection, the copper versenate achieved a concentration in metastatic tumors about nine times, and in more rapidly growing gliomas about five times, that in normal brain. Concentrations of copper in muscle rose steadily, whereas those in tumor and normal brain fell. As with other isotopes, high uptake by the muscle in the temporal and suboccipital regions obscured, in these areas, diagnostic concentrations recognizable elsewhere in the brain.

Copper scanning, best carried out within an hour of intravenous injection, detected about 55 per cent of a random series of 29 intracranial tumors. In the same patients, arsenic scans detected 76 per cent of the tumors. Some tumors, however, were detected by copper in which arsenic failed. Vascular lesions (15 cases scanned with both isotopes) are less likely to yield a positive scan with copper than with arsenic.

About 5 per cent of an intravenously injected dose of copper versenate is excreted in the urine. The rest largely undergoes physical decay of its activity before excretion occurs.

The copper-64 injected for a diagnostic scan gives a whole-body radiation dosage of 0.33 rad, which is about the weekly permissible dose for personnel constantly exposed to radiation. Hence this diagnostic maneuver may be repeated several times with impunity.

Eight figures; 4 tables.

EUGENE A. CORNELIUS, M.D.  
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**Diagnosis of Diseases of the Mammary Gland.** E. D. Shibaeva. *Vestnik rentgen. i radiol.* 33: 32-35, November-December 1958. (In Russian) (Rostov-on-Don, Russia)

The author has studied two accessory methods of

examining the mammary gland. The first was by means of plain films of the breast; from his series of 107 patients he concluded that the mammary gland gives characteristic patterns in a number of diseases.

The second method consists in diagnosing malignant tumors of the mammary gland with radioactive phosphorus, which is concentrated selectively in spleen, bone, and rapidly growing tumor tissues. Radioactive phosphorus was administered to 27 women with breast tumors. Histologic examination of the tumors eventually showed 18 to be malignant; 3 were fibroadenomas; 6 were fibrocystic adenopathies. A beta counter used twenty-four hours after the administration of the isotope revealed a count of between 100 and 125 per cent of normal in benign tumors, with the other breast as a control; in malignant conditions the count was between 125 and 250 per cent of normal.

B. ABRAHAMSON, M.D.  
F. RIEBEL, M.D.  
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**The Use of Iodine 132 for Thyroid Function Tests.** K. E. Halnan and E. E. Pochin. *Brit. J. Radiol.* 31: 581-588, November 1958. (Department of Clinical Research, University College Hospital Medical School, London, England)

The chief advantages of  $I^{132}$  compared to  $I^{131}$  for study of thyroid function are reduction in radiation dosage both to the thyroid and gonads and the fact that tests may be repeated at short intervals, reliably and conveniently. This latter advantage is attributable to the much shorter half-life of  $I^{132}$  (two to three hours). The higher beta and gamma emissions afford equal or higher sensitivity for counting systems, yet the total dosages will be lower than with  $I^{131}$ .

Various investigations were performed on normal and pregnant subjects and on hypothyroid, hypopituitary, and breast cancer patients, and the responses to various hormone preparations are described. The authors suggest the neck-thigh ratio two hours after an oral dose of  $I^{132}$  as a convenient measurement of thyroid function.

Twelve graphs, 3 tables.

MAJ. H. N. STURTEVANT, M.C.  
Lackland AFB, Texas

**The Use of Iodine 132 in Studies of Thyroid Function.** A. W. C. Goolden and J. R. Mallard. *Brit. J. Radiol.* 31: 589-595, November 1958. (M. R. C. Radiotherapeutic Research Unit and Physics Department, Hammersmith Hospital, London, W. 12, England)

The authors have used  $I^{132}$  in experimental investigations of variations of thyroid function and of the effect of drugs on thyroid activity. They have also employed it in conjunction with  $I^{131}$  to investigate the mechanism of suppression of thyroid function in response to the administration of triiodothyronine.

As a tracer for clinical use,  $I^{132}$  has the advantage that the radiation delivered to the thyroid by an equivalent dose is only about one-thirtieth that of  $I^{131}$ , an amount which is further decreased since the radioactivity stored in the gland is limited by the rapid decay of the isotope.  $I^{132}$  is therefore especially suitable for tests in pregnant women and in children and can be used for successive tests on the same patient without exceeding the permissible radiation dose. Among disadvantages of  $I^{132}$  are its relatively greater cost as



compared to  $I^{131}$ , and the time required for preparation of the dose and calculation of the results.

The authors have not used  $I^{132}$  in the routine testing of thyroid function, nor do they consider it likely to replace  $I^{131}$  in standard diagnostic work. They have, however, found it most useful in the experimental studies of thyroid metabolism.

Eleven graphs; 2 tables.

**The Effect of Food on the 3-Hour Thyroidal Uptake of  $I^{131}$  in Human Subjects.** David J. Turell, Arthur S. Littell, and Richard P. Levy. *J. Clin. Endocrinol.* **18**: 1029-1032, September 1958. (Western Reserve University, Cleveland 6, Ohio)

Previous observations have indicated that the presence of food in the stomach delays the absorption of iodide by the thyroid gland and patients have therefore been fasted before the administration of  $I^{131}$  tracers, as for the thyrotropin stimulation test. To determine the validity of this view, the three-hour thyroidal  $I^{131}$  uptake was studied in 22 fasting and in 18 lightly fed subjects. No significant change in uptake was demonstrated. It is concluded, therefore, that patients may eat a light breakfast before thyroidal  $I^{131}$  uptake studies involving periods of three hours or longer.

**The Influence of Age on Excretion of Radioactive Iodine.** G. A. MacGregor and H. Wagner. *Lancet* **2**: 612-614, Sept. 20, 1958. (G. A. M., St. Luke's Hospital, Warren Rd., Guildford, Surrey, England)

Measurement of the urinary excretion of radioactive iodine ( $I^{131}$ ) has proved valuable in the diagnosis of hyperthyroidism. Because it was suspected that this test was not as reliable in elderly as in younger patients, the results in 197 euthyroid patients (147 female, 50 male), ranging from twenty to eight-two years of age were reviewed.

The excretion test as routinely employed calls for the collection of urine during three periods in the forty-eight hours following the administration of the  $I^{131}$ . The percentage of the dose excreted during the 0-8-hour period, the 8-24-hour period, and the 24-48-hour period is measured, and a thyroid-uptake or "T" index is calculated from the formula

$$T = \frac{(0-8) \text{ hours, } \% \times 100}{(8-24) \text{ hours, } \% \times (0-48) \text{ hours, } \%}$$

This procedure gives results relatively independent of renal function. The currently accepted normal range of the T-index is 2.8-13.

The results in the series of 197 euthyroid patients were analyzed by plotting the T-index and the excretion values for the individual urine-collection periods against the patient's age. The T-index was found to decrease with advancing age. This was shown by the calculated regression line, which had a slope of  $-0.065$  T-units per year of age ( $P < 0.001$ ). The correlation coefficient of the T-index with age is  $-0.42 \pm 0.07$ . The distribution of the points suggests that the relationship between the T-index and age may be curvilinear rather than linear. A significant decline was also obtained when  $\log T$  was plotted against age, and the  $\log T$ -age regression line was used in calculating the limits of normality. Ninety-five per cent of the values lie within these limits.

The rate of decline of the accumulation gradient with age observed by Perlmutter and Riggs (*J. Clin. Endocrinol.* **9**: 430, 1949. *Abst. in Radiology* **54**: 638, 1950) closely resembles that of the T-index in the

present series. The authors' data suggest that in patients over fifty, results in the "upper normal" range (T-index 9-13) may indicate hyperthyroidism.

Two graphs; 1 table.

**A Modification of the  $I^{131}$  Triolein Test of Fat Absorption Utilizing a Capsule Test Meal.** J. K. Isley, Jr., A. P. Sanders, G. J. Baylin, J. M. Ruffin, W. W. Shingleton, W. G. Anlyan, and K. W. Sharpe. *Gastroenterology* **35**: 482-484, November 1958. (Duke University Medical Center, Durham, N. C.)

A simplification of the fat absorption test originally described by the authors (Baylin *et al.*: *Proc. Soc. Exper. Biol. & Med.* **89**: 51, 1955) is offered. This consists in the substitution of a capsule containing fat for the emulsion type test meal.

Thirty-nine normal adult persons were used as controls in this study. They were subdivided into groups A and B. The 26 controls in group A were fasted for six hours preceding the test and for the initial six hours of the test. Each subject was then given one capsule containing 25 microcuries of  $I^{131}$ -labeled glycerol trioleate, mixed with peanut oil to a total volume of 0.5 ml. Three 0.5-ml. gelatin capsules containing barium sulfate and one capsule containing sodium iodide crystals were given at the same time. Blood samples were drawn at the fourth, fifth, and sixth hours after administration of the capsules. Each sample was analyzed for radioactive content and the percentage of administered radioactivity in the blood present at the time the sample was taken was then determined by the technic described by Baylin *et al.* in their earlier report.

At the end of three hours the patients were fluoroscoped or a radiograph of the abdomen was taken to determine gastric emptying and to confirm dissolution of gelatin capsules.

Group B was composed of 13 normal subjects. There was no specific preparation for the test. Each member of the group was given one capsule containing neutral fat, as previously described. The stools were collected for a period of forty-eight hours and the fecal recovery of ingested material was determined for each subject.

Twenty-four normal dogs were evaluated by the capsule technic as to their absorption of glycerol trioleate. The test on the animals was performed in a similar manner to that described for the human subjects except for fecal collections.

A group of abnormal patients with previously diagnosed gastrointestinal disease (pancreatectomy, regional enteritis, and Whipple's disease) and a group of abnormal dogs were also studied by this method.

The authors present tables and charts which seem to establish definitely that the capsule can be substituted for the more elaborately prepared fat emulsion and give comparable results. It is felt the ease with which a capsule type of test-meal can be prepared should better enable the smaller isotope laboratories to take advantage of this diagnostic procedure.

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**Thyroxine Metabolism in Man Estimated by Means of  $I^{131}$ -Labelled L-Thyroxine.** Thorkild Friis. *Acta endocrinol.* **29**: 587-601, December 1958. (København Apts Sygehus, Gentofte, Denmark)

The purpose of the study reported here was in part to test the statement of Ingbar and Freinkel (*J. Clin. Invest.* **34**: 1375, 1955) that strumectomized patients



with Graves' disease continue to show an increased thyroxine metabolism, even though euthyroid, and in part to determine the thyroxine metabolism in hypometabolic patients with normal thyroid function and in patients with hepatitis. Thirty-one patients were investigated: 7 persons suffering from disorders which presumably were not related to the thyroxine metabolism (fibrositis, neurasthenia), 3 thyrotoxic, 1 myxedematous, 3 hypermetabolic and euthyroid, 6 hypometabolic, 5 strumectomized patients who were euthyroid, and 6 with acute or subacute hepatitis.

In the hypermetabolic and the strumectomized patients the thyroxine metabolism did not differ from the normal, where the biological half-life of thyroxine in plasma has been found to vary from seven to nine days. It was shortened in the thyrotoxic patients and in those with hepatitis, prolonged in 4 out of 6 hypometabolic patients and in 1 patient with myxedema.

It was found in supplementary investigations that about 25 to 30 per cent of the activity is localized at once in the liver, about 20 to 30 per cent is excreted in the urine, and about 10 per cent in the feces in the course of ten days. In the patients with hepatitis rather less of the activity is accumulated in the liver, and somewhat more is apparently excreted in the feces.

In all the patients, only radioactive iodide, but no thyroxine, was present in the urine.

Five figures; 5 tables.

**Iodine Metabolism of Endemic Goiter on the Åland Islands (Finland).** B.-A. Lamberg, Peter Wahlberg, Otto Wegelius, Gunnar Hellström, and P. I. Forsius. *J. Clin. Endocrinol.* 18: 991-1005, September 1958. (Fourth Medical University Clinic, Helsinki, Finland)

Studies of the urinary excretion of radioactive iodine and stable iodine, of the concentration of protein-bound iodine in serum, and calculation of the daily production of thyroid hormones, together with clinical investigation, were carried out in 130 subjects who had lived on the Åland Islands all their lives, though some of them had spent a year or two elsewhere.

The following observations were made: (1) With respect to the incidence of nodularity (86 per cent), the endemic goiter on the Åland Islands is comparable with that on the Finnish mainland. (2) In normal subjects, the average forty-eight-hour excretion of radioactive iodine was 49.3 per cent of the administered dose. (3) The daily urinary excretion of stable iodine (corrected for methodologic error) was about 49.5  $\mu$ g. (4) With increasing size of the thyroid gland there was a statistically significant decrease in the excretion of radioactive iodine; in the group with the largest goiters this excretion was only 32.2 per cent. (5) In normal subjects the calculated daily production of thyroid hormones was the equivalent of about 62.5  $\mu$ g. of iodine per day (corrected for methodologic error); it rose with increasing thyroid volume to a level of about 124.5  $\mu$ g. per day for the group with the largest goiters, a value which differed significantly from that for the control group.

A relatively or absolutely diminished availability of iodine to the thyroid, evidently resulting from deficient intake of iodine, plays a significant part in the development of goiter on the Åland Islands. The increased daily production of thyroid hormones in the goiter group can be explained by an increased re-utilization of the iodine liberated.

A comparison is made of the pattern of iodine me-

tabolism in the Åland Islands and other areas where goiter is endemic.

Four figures; 2 tables.

**Metabolism of Progesterone-4-C<sup>14</sup> in a Postmenopausal Woman with a Biliary Fistula.** W. G. Wiest, G. I. Fujimoto, and A. A. Sandberg. *J. Clin. Endocrinol.* 18: 972-980, September 1958. (University of Utah College of Medicine, Salt Lake City, Utah)

The distribution of radioactivity in bile and urine after injection of progesterone-4-C<sup>14</sup> was studied as a function of time in a normal postmenopausal woman with a biliary fistula. The amounts of methylene chloride-soluble ("free") steroid and the material which became chloroform-soluble after hydrolysis with  $\beta$ -glucuronidase were measured and analyzed by paper chromatography. The major amount of radioactivity was excreted in the bile. Both bile and urine contained pregnanediol, pregnanolone, and some unidentified polar material, all of which were released by  $\beta$ -glucuronidase hydrolysis. Characterization of pregnanediol and pregnanolone was based on chromatographic mobility and carrier experiments using authentic steroids.

Four figures; 2 tables.

AUTHORS' SUMMARY

**Collective Review: Studies of the Resorption of Chromium-51 Tagged Erythrocytes from the Peritoneal Cavity; the Absorption of Fluids and Particulate Matter from the Peritoneal Cavity.** Donald B. Rochlin, Harry Zill, and William S. Blakemore. *Surg., Gynec. & Obst. (Internat. Abst. of Surg.)* 107: 1-14, July 1958. (University of Pennsylvania, Philadelphia 4, Penna.)

An experimental re-evaluation of intraperitoneal transfusion was undertaken in order to determine the feasibility of this route of transfusion when selected for use in unusual clinical situations. The experiments were performed on dogs and the blood for transfusion was labeled with chromium 51. A further application of this work concerns itself with the resorption of blood left in the abdominal cavity following trauma or abdominal operations.

Approximately 70 per cent of the volume of blood injected intraperitoneally was found in the blood stream of animals that were transfused with varied volumes of red cell suspension. The maximum concentration of the transfused cells in the blood stream occurred forty-eight to ninety-six hours after the injection. This was equal to the percentage of the blood volume found at a comparable time after intravenous transfusion.

No significant differences could be found between the survival time of intraperitoneally transfused erythrocytes and that of erythrocytes transfused intravenously.

Experimental data strongly suggest that the resorption from the peritoneal cavity occurs entirely via the lymphatics, and that passage of the erythrocytes directly into the blood stream via the capillaries is improbable.

Since the total percentage of resorption remained relatively constant in spite of wide differences in the total lymph volume, the rate of resorption of erythrocytes from the peritoneal cavity probably does not vary directly with the volume of lymphatic drainage from the thoracic duct.

Eleven figures; 3 tables.

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**Studies to Detect the Escape of Amniotic Fluid into the Maternal Circulation During Parturition.** Richard A. Sparr and Jack A. Pritchard. Surg., Gynec. & Obst. 107: 560-564, November 1958. (University of Texas Southwestern Medical School, Dallas, Texas)

The syndrome of amniotic fluid embolism occurs in parous women in whom there is a rupture of the amniotic sac associated with forceful uterine contractions. Amniotic fluid, with its particulate matter, consisting of fetal squamous epithelial cells, hairs, and vernix, presumably enters the maternal circulation through incomplete uterine or cervical lacerations or at sites of placental separation. In some instances the clinical manifestations are unconsciousness, convulsions, cyanosis, and shock, followed rapidly by death. In others there may be massive hemorrhage from the genital tract, from the operative field, or from any site of trauma, heralding the development of hypofibrinogenemia or other abnormalities in the hemostatic mechanism. A third complication, usually related to subclinical amniotic fluid embolism during labor and delivery, is the delayed appearance of primary pulmonary hypertension with pulmonary arterial and arteriolar sclerosis, characterized by fibrosis and hyalinization of the arterial wall and endarteritis obliterans in response to the amniotic foreign body material entrapped in these vessels.

Two cases are reported. In one the patient expired almost immediately. In the other, death did not occur until four and a half hours after the initial evidence of difficulty and defective blood coagulation was demonstrated. In both, histologic study revealed the classic picture of fetal squamæ and mucin in the arterioles of the lungs.

A study was then undertaken to determine whether moderate amounts of amniotic fluid regularly or occasionally escape into the maternal circulation without producing symptoms and whether the detection of any amniotic debris in the maternal blood vessels is always an indication of a pathologic state. Since repeated mention has been made of the possible etiologic role played by pitocin in the production of amniotic fluid embolism, special attention was directed to this point.

Maternal erythrocytes labeled with radioactive sodium chromate ( $\text{Na}_2\text{Cr}^{51}\text{O}_4$ ) were introduced transabdominally into the amniotic sac prior to labor and delivery to serve as a "tag" and the maternal blood was checked for the appearance of radioactivity during and after labor and delivery. If any amniotic fluid entered the maternal circulation, it could be detected by the tagging. The patients selected for study were candidates for repeat cesarean section (13 patients) or were at term, either in early labor or suitable for induction of labor (25 patients). Spontaneous labor with delivery occurred in 13 of the series, and labor was induced and maintained with diluted intravenous pitocin solution in 12.

It is concluded, on the basis of these studies, that normally, practically no amniotic fluid escapes into the maternal circulation during labor or at delivery, that the use of pitocin to initiate and maintain labor does not enhance its escape, and that the finding of any amniotic fluid debris in the maternal lungs is evidence of a pathological process rather than merely an aftermath of normal labor and delivery.

One photomicrograph.

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**Theoretical Study of Dosage and Geometric Distribution of Radioactive Gold Seeds in Interstitial Radiotherapy.** A. Bercy and A. Delferière. J. belge de radiol. 41: 221-240, 1958. (In French)

**Irradiation of Tumors with Gold Seeds. Simplification of Calculation.** A. Bercy. J. belge de radiol. 41: 729-735, 1958. (In French) (Université de Liège, France)

The implantation of radioactive gold seeds in tumors permits homogeneous irradiation, but the pattern of distribution of the seeds, as well as their strength, must be varied according to the surface area and the volume of the tumor. Irradiation charts have been established whereby the seed strength for any surface or any volume may be calculated and the distance between the individual seeds determined in order to obtain 6,000 r as a maximum or a minimum dose.

In the second of the two papers listed above, Bercy presents two graphs to simplify the determination of the number of implants of 5, 4, or 3 mc strength required for implantation into a tumor of given volume.

The graphs give the distance between the seeds for a minimum dose of 6,000 r. There is also a corrective factor which may be applied if the tumor is not more or less cubical; this is called the factor of elongation.

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**Treatment of Lung Tumors with a Radioactive Gold-Carbon Suspension; Animal Experiments.** Helmut Ernst, Eduard Iglauer, Helmut Kronschwitz, and Ernst Spode. Strahlentherapie 107: 382-390, November 1958. (In German) (Institut für Medizin und Biologie der Deutschen Akademie der Wissenschaften zu Berlin, Germany)

The authors conducted experiments on 18 dogs using a radioactive gold-carbon suspension introduced by a method previously described by Muller and Rossier (Acta radiol. 35: 449, 1951. Abst. in Radiology 58: 626, 1952). The solutions consisted of colloidal radioactive gold, charcoal particles measuring from 30 to 50 micra, glucose, pectin, and the animal's own blood. This was introduced through a cardiac catheter into the jugular vein or one of the pulmonary arteries. The animals were killed from one to thirty days after the injection. Radioautographs and scintigrams were obtained to check the distribution of the radioactive material.

It was found that after twenty-four hours, 70 per cent of the injected material was present in the lungs. Of the remainder, the largest quantities were in the liver and spleen. There was excellent and homogeneous distribution of the radioactive gold in the various lung tissues; only a few of the charcoal particles were found in the hilar lymph nodes.

On the basis of their observations on animals, the authors conclude that this type of selective irradiation of certain portions of the lungs should be of definite value in the treatment of lung cancer.

Five figures; 4 tables.

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**Internal Irradiation of Dogs with Radioactive Colloidal Gold: Synergistic Effect of Iron.** P. F. Hahn and H. C. Meng. Cancer 11: 591-596, May-June 1958. (P. F. H., Meharry Medical College, Nashville, Tenn.)

The role played by iron in the formation of fibrous

tissue in the liver or, conversely, the effect of fibrosis on the deposition of iron in hepatic tissue in hemochromatosis has never been explained. The authors describe an investigation of the influence of iron deposits in the liver upon the effect of internal irradiation in the dog. In the first series of experiments, dogs were given 60 mg. of iron (ferrous gluconate) intravenously for thirteen days prior to the administration of  $Au^{198}$ . In subsequent series, iron was given intravenously in the form of saccharated iron oxide (Feojectin) at a dose level of 100 mg. per day for varying periods (seven to thirteen days) before or concomitant with the first injection of  $Au^{198}$ . The radiogold was given intravenously in doses delivering 7,000 to 15,000 rep each to the liver, for a total of 37,000 to 77,000 rep. The effect of  $Au^{198}$  upon the liver was found to be heightened by the previous administration of iron; this was particularly evident when the iron was given intravenously in particulate form, with resultant deposition in the reticuloendothelial system. Ascites as well as moderately extensive cirrhotic changes in the liver developed in animals given iron in addition to  $Au^{198}$ .

Transient but marked leukopenia was observed in dogs receiving  $Au^{198}$  alone. Erythropoiesis was not noticeably influenced, but precipitous drops in hematocrit levels that corresponded to massive internal hemorrhage occurred terminally.

Alterations in electrophoretic patterns of plasma were essentially the same for the dogs that received both  $Au^{198}$  and iron as in those which received internal irradiation alone. There was a decided lowering of the albumin-globulin ratio as a result of lowered albumin levels. The beta globulins were considerably increased, as were the gamma globulins. Total proteins were not markedly affected.

Four tables.

**Turnover Studies with  $^{59}Fe$  in the X-Irradiated Rat.** E. H. Belcher, Eileen B. Harriss, and L. F. Lamerton. *Brit. J. Haematol.* 4: 390-403, October 1958. (E. B. H., Royal Cancer Hospital, Belmont, Surrey, England)

This article reports a continuation of a previous study on distribution of radioactive iron,  $Fe^{59}$ , injected subcutaneously into x-irradiated rats (*Brit. J. Haematol.* 1: 86, 1955. *Abst. in Radiology* 65: 830, 1955). The earlier investigation showed that recovery from radiation-induced anemia in rats given 450 r x-radiation was initially due to increased splenic erythropoiesis, and that recovery of erythropoietic function in bone marrow occurred later than in the spleen. The pattern of recovery could be modified by shielding one hind limb during irradiation, the shielded limb then having an initially enhanced erythropoietic activity which was not maintained, and the spleen becoming highly erythropoietic at an earlier time than in animals receiving whole-body irradiation.

In this early work  $Fe^{59}$  uptake in bone marrow was studied in the bones of the hind limbs only. Detailed studies have now been made of  $Fe^{59}$  distribution and turnover in all tissues of unirradiated and whole-body irradiated rats in order to determine the validity of the use of the turnover of the isotope by the hind limb as an index of bone marrow erythropoietic function. Turnover was also studied in detail in selected tissues of rats given 200 r or 450 r x-radiation with or without hind-limb shielding, in order to determine more accurately the maximum uptake levels attained and to

obtain a more complete picture of the effects of hind-limb shielding on the response of the erythropoietic tissues to x-radiation.

The data obtained abundantly confirm the results of the earlier distribution studies. First, the important role played by the spleen during recovery of the erythropoietic system from radiation damage is again demonstrated. Thus, in recovery from 450 r whole-body irradiation, the spleen at first plays the major erythropoietic role, and recovery of erythropoiesis in the bone marrow does not occur until some days after recovery in the spleen. Secondly, the far-reaching effects which follow shielding of a small portion of active bone marrow are confirmed. Thus, shielding one hind limb during irradiation at 450 r results in an initially enhanced erythropoietic activity in the shielded limb, although this is not maintained. An abortive rise in erythropoietic activity in the unshielded bone marrow then occurs followed by an earlier rise in splenic erythropoiesis than is observed in animals receiving whole-body irradiation.

The significance of these findings and the protective mechanisms involved are discussed.

Sixteen figures; 3 tables.

**Studies on the Anemia of Tumor Bearing Animals. I. Distribution of Radioiron Following the Injection of Labeled Erythrocytes.** Robert E. Greenfield, Jamie E. Godfrey, and Vincent E. Price. *J. Nat. Cancer Inst.* 21: 641-656, October 1958. (National Cancer Institute, Bethesda, Md.)

Iron distribution studies on rats bearing certain transplanted tumors indicated that the tumors contained large amounts of iron, frequently exceeding the total amount of iron found in the liver. Following the intravenous injection of  $Fe^{59}$ -labeled red cells into normal and tumor-bearing rats and mice, the  $Fe^{59}$  concentration decreased at a more rapid rate in the tumor-bearing animals. The rate at which the  $Fe^{59}$  concentration decreased, and the time after implantation of the tumor when the decrease started, varied markedly from tumor to tumor. The rate at which the  $Fe^{59}$  left the blood of any single tumor-bearing animal varied randomly from day to day. The tumor-bearing animals frequently had larger blood volumes than their normal controls. In some instances the increased blood volume was associated with an increased total body weight. In no instance did the change in blood volume more than partially account for the decrease in the concentration of labeled erythrocytes observed in the circulating blood of the tumor-bearing animals.

A study of the distribution of  $Fe^{59}$  in the normal and in the tumor-bearing rats revealed that a high proportion of the  $Fe^{59}$  which had left the blood stream could be found in the area of the tumor. The loss of  $Fe^{59}$ -labeled erythrocytes from the blood stream was correlated with the amount of  $Fe^{59}$  in the tumor, the onset of anemia, and the development of cachexia in the host.

Three figures; 6 tables.

Authors' Summary

**Tantalum 182 in the Treatment of Bladder Tumors.** Gösta Jönsson, Bror Månsson, and Lars Röhl. *Acta chir. scandinav.* 115: 111-119, 1958. (University of Lund, Lund, Sweden)

Between May 1, 1955, and Nov. 1, 1957, 63 patients with bladder tumors were treated by surgery and

irradiation at the University of Lund. Ta<sup>182</sup> was implanted intravesically in all cases, usually following partial cystectomy (in 47 of the 63 cases). This operation was combined with ureteral transplantation in 25 cases and with prostatectomy in 2 cases. Cystostomy with tantalum implantation was done in 9 cases and excision in 7. The tumors were grouped histologically. Benign papilloma (21 cases) constituted Group I; differentiated transitional-cell carcinoma (23 cases) Group II; undifferentiated transitional-cell carcinoma (19 cases) Group III. All of the tumors in Group I were confined to the mucosa. Sixteen of those in Group II involved only the mucosa, 5 had infiltrated into the muscle coat, and 2 had grown transvesically and perivesically but were not fixed to the pelvic wall. Six of the tumors in Group III had infiltrated into the muscle coat, 10 had grown transvesically and perivesically but were not fixed to the pelvic wall, and 3 showed transvesical and perivesical growth with fixation. Preoperative biopsy was seldom performed as, in the writers' opinion, the relation of the tumor to the bladder wall cannot always be established by biopsy and the procedure involves risk of implantation metastases.

There were no deaths attributable to surgery. The tantalum needles employed were 12.5 cm. long and generally had an activity of 12 to 13 mc each when delivered from the reactor, corresponding to about 1 mc Ta<sup>182</sup> or 0.75 mg. Ra per linear cm. The technic of implantation was that described by Wallace *et al.* (Brit. J. Radiol. 25: 421, 1952. Abst. in Radiology 60: 928, 1953) [and the needles were presumably of hairpin shape, though this is not stated]. If only one needle was implanted, the dose was calculated at a point symmetrically situated between the branches. If more than one needle was used, the dose was always determined between the branches of each separate needle and also between the adjacent branches of different needles. Treatment periods ranged from three days, with a dose of 4,620 r, to fifteen days with 8,300 r. As a rule, treatment was given for five to eight days, and the dose was 5,500 to 6,500 r. The irradiation reaction in the bladder and the subjective distress were brief and mild in the patients with benign papilloma. No recurrence *in loco* or elsewhere appeared during follow-up in this group. In Groups II and III the reaction was intensified, as was to be expected, since the dosage and extent of bladder resections were greater than in Group I. Ten patients have died, 2 from Group II and 8 from Group III. In almost all, there had been perivesical extension of cancer at the time of operation.

On the basis of their results, the authors conclude that it is warrantable to perform such a radical operation as partial cystectomy plus implantation of Ta<sup>182</sup> even in benign, large papillomas, but the procedure should be reserved for tumors which have not infiltrated through the bladder wall.

Two roentgenograms; 2 charts.

**The Response of Dogs to Bilateral Whole-Body Co<sup>60</sup> Irradiation. I. Lethal Dose Determination.** James N. Shively, Sol M. Michaelson, and Joe W. Howland. Radiation Res. 9: 445-450, October 1958. (University of Rochester School of Medicine and Dentistry, Rochester, N. Y.)

This investigation was initiated to supply mortality information pertaining to dogs exposed to Co<sup>60</sup> gamma radiations for use as a basic value to which other studies in the same laboratory might be related.

Young adult dogs were exposed to single bilateral doses of Co<sup>60</sup> gamma rays. The midline tissue LD 50/30 was 335 r. This dose is essentially the same as for unilateral 250-kvp x-irradiation applied to the dorsal aspect (Radiation Res. 4: 139, 1956. Abst. in Radiology 68: 316, 1957).

The earliest deaths occurred in the 436-r group, with 3 dogs dying on the twelfth day after irradiation. The latest deaths were in 2 animals in the 292-r group, which died on the twenty-fourth and twenty-fifth post-irradiation days, respectively. The mean day of death for all groups was 17.3 days. The mode and median were both seventeen days. Statistical analysis showed a highly significant difference in mean survival between the 436-r and 292-r dose groups. All other group comparisons, except that between the 336-r and 385-r groups, indicated significant differences.

A study of the cumulative mortality curves by days suggests an inverse relation between the day of first death in group and dose.

Statistically significant differences in the mean per cent weight loss of decedent animals were found when either high-dose group (385 r, 436 r) was compared with either low-dose group (292 r, 336 r).

**Study on the Exchangeability of Sodium and Potassium by Their Isotopes in Clinical Conditions.** J. C. Demanet, E. Engel, and R. S. Mach. Schweiz. med. Wchnschr. 88: 1180-1185, Nov. 22, 1958. (In French) (Institut du Radium, Hôpital cantonal, Geneva, Switzerland)

The methods employed in determining the exchangeability of sodium and potassium by their isotopes in clinical conditions are outlined and the results obtained in studies of normal, potassium-depleted, and edematous patients are noted.

The mean obtained among normal males was  $53 \pm 5.1$  mEq./kg. for exchangeable potassium ( $K_e$ ) and  $43.3 \pm 5.2$  mEq./kg. for exchangeable sodium ( $Na_e$ ). Among normal women the mean was  $42.1 \pm 6.8$  mEq./kg. for  $K_e$  and  $39.1 \pm 4.7$  mEq./kg. for  $Na_e$ . If the patients, male and female, are put into three categories according to the degree of edema, the results read: mean values for  $Na_e$   $45.3 \pm 7.1$  mEq./kg. in cases of discrete edema;  $53.9 \pm 9.3$  mEq./kg. in cases of peripheral edema;  $66.8 \pm 7.5$  mEq./kg. in cases of anasarca. Low values of  $K_e$  (24.7 and 31.2 mEq./kg.) were found in 2 cases of potassium depletion.

The faithfulness and precision of the methods used are shown by a percentage error (fractional standard deviation) of  $\pm 1.66$  per cent for the  $Na_e$  and  $\pm 3.78$  per cent for the  $K_e$ .

Six figures; 5 tables.

**Study on the Variations of the Exchangeability of Sodium by Radiosodium in the Course of Treatment of Edema; Comparison with the Balance Method.** J. C. Demanet, R. Collet, E. Engel, and R. S. Mach. Schweiz. med. Wchnschr. 88: 1185-1187, Nov. 22, 1958. (In French) (Institut du Radium, Hôpital cantonal, Geneva, Switzerland)

The variations of the exchangeability of sodium by radiosodium in the course of the treatment of edema were studied in comparison with external sodium balance determinations in 5 patients, 4 of them with edema. Sixteen comparative studies showed a difference of  $13 \pm 48$  mEq. between the values obtained by the two methods, a very good correlation.



These experiments permit the following conclusions:

(1) If attention is paid to the modification of sodium retention as shown by the balance study, the determination of exchangeable sodium in edematous patients is as exact as that among normal subjects.

(2) With the repetition of the determination of ex-

changeable sodium, it is possible to control the sodium balance study and to replace it during a prolonged metabolic study. The radiosodium technic has the advantage of being more exact because it is not subject to the accumulation of errors found in the external balance method.

## RADIATION EFFECTS

**The Hazards of Ionizing Radiation.** A. Zuppinger. Schweiz. med. Wchnschr. 88: 1171-1179, Nov. 22, 1958. (In German) (Röntgeninstitut der Universität Bern, Switzerland)

The author reviews some of the commonly accepted observations on biological radiation hazards.

Total exposure is, comparatively speaking, much more dangerous than local exposure. In man, 400 r produce 50 per cent mortality and 200 r increase the leukemia-expectancy rate tenfold. Treatment of excessive exposure is as yet undeveloped, and the acute radiation syndrome after total exposure must be treated symptomatically.

Genetic damage should be considered the greatest radiation hazard, not so much for the isolated individual as for the gene composition of the whole population. Genetically speaking, there is probably no permissible exposure and no recovery factor. Thirty to 40 r doubles the gene mutation rate in man. Damage to the embryo occurs through a combination of somatic and genetic influences and is most severe in the first two months of pregnancy.

Variations in the blood formula are not characteristic after small exposures and are useless as indicators of minor radiation damage. Radiation skin cancers always appear at the site of chronic dermatitis, and chronic ulcers should be considered precancerous. Radiotherapy of thymus hyperplasia is permissible only when there is a threat of suffocation, as this treatment raises the leukemia-expectancy rate three to four times.

Man is exposed to an average of 100 mr yearly from natural sources, and prudent estimates consider that double this dose would be tolerated. The increase due to the development of atomic energy can be maintained within permissible limits in peacetime.

Medical, especially diagnostic, radiography is the largest source of excess radiation. Six to eight pelvic examinations account for three-fourths of the total exposure dose. An exact posing of the clinical problem is a useful means of decreasing exposure. The field of examination should be limited to the minimum compatible with solution of this problem. Exposure to the gonads can be reduced by the use of limited fields. Special care in this respect must be taken with children and pregnant women. "Hard ray" technic decreases the gonadal exposure considerably when the gonads are in the field.

Fluoroscopy is a greater hazard than radiography but remains an acceptable method of examination.

As far as permissible exposures are concerned, a differentiation should be made between the whole population and the radiation personnel. The latter can remain well within the maximum permissible limits and it is even possible that their exposure can be maintained within the same limits as that of the population as a whole, if there is good order and discipline in their work.

Prophylactic chemical radiation protection is definitely possible with different products, above all with S-H-containing substances.

Two figures; 2 tables.

**Radioactivity and the Human Skeleton.** Janeway Lecture, 1958. L. D. Marinelli. Am. J. Roentgenol. 80: 729-739, November 1958. (Argonne National Laboratory, Lemont, Ill.)

The author states it as his object to outline a few salient points as to what has been done and what remains to be done in the direct appraisal of the cancerogenic expectations from deposition of radium in bone as an aid in predicting the possible effects of low concentrations of radioactive material in the human skeleton accumulated as by-products of nuclear detonations. The radium contents of human skeletons (from water and food intake) in various geographical areas are plotted against the bone tumor incidence; the skeletal radium content and tumor incidence provide preliminary data concerning the probable incidence of bone cancer and reflect some data on permissible bone levels, but the findings are statistically uncertain. For analysis at a higher level, the author turns his attention to the radium dial painters. Two other groups of persons are also considered: those injected with Thorotrast for diagnostic purposes many years ago and Indian and Brazilian populations living over thorium-containing sands. More complete surveys of patients and populations subjected to exposures to Thorotrast or natural and industrial thorium are yet to be made.

The investigation shows a direct relationship between bone cancer incidence and the skeletal dose of Ra 226 and Ra 228. The incidence of bone cancer is plotted graphically against the total radiation dose of constant Ra 226 burden (data collected from various geographical areas and from dial painters). A task of great magnitude remains in the analytic investigations of the long-term effects of radiation and determinations of permissible levels of exposure.

Two graphs; 4 tables. JOHN W. WILSON, M.D.  
Johnstown, Penna.

**Leukemogens.** John D. Abbatt and A. J. Lea. Lancet 2: 880-883, Oct. 25, 1958. (J. D. A., General Electric Co., Atomic Energy Division, Erith, Kent, England)

The production of leukemia by radiation has received so much publicity in recent years that "radiation" and "leukemia" have become very closely associated. While in no way wishing to underestimate the importance of radiation, the authors feel that this publicity has perhaps caused other possible factors in the production of leukemia to be overlooked. They have therefore used a large series of cases of leukemia to investigate other possible leukemogenic factors which



have from time to time been suggested, but for which, as far as could be ascertained, no firm supporting evidence relating to man has ever been provided.

A series of 679 cases of leukemia were obtained from the records of the Ministry of Pensions and National Insurance. Two control series, one of all diseases and injuries, the other of neoplasms other than the reticuloses, consisting of 813 and 554 cases respectively, were secured from the same source. The incidence in these series of various factors alleged to be leukemogenic were compared.

The results furnish no evidence whatever in support of the suggestions that fractures, injuries other than fractures, antibiotics (penicillin), or chronic sepsis are related to the onset of leukemia. On the other hand some form of association was found between leukemia and (a) radiation and (b) rheumatic diseases. Radiation is known to be leukemogenic, and it would have been surprising if no association had been demonstrated. The validity of the results derived from the material used in this investigation is discussed in some detail.

The authors have stated previously (Lancet 2: 1317, 1956. Abst. in Radiology 70: 152, 1958) that they consider radiation to play a major part in the production of leukemia in irradiated cases of ankylosing spondylitis. They still believe this to be true, but the present evidence indicates that the other rheumatic diseases are also associated with the incidence of leukemia. This, in their view, precludes the use of such cases in radiation-induced leukemia dose-response investigations.

While the evidence does show some form of association between leukemia on the one hand and rheumatic diseases and irradiation on the other, it does not supply an explanation of these associations.

Four tables.

**Acute Leukaemia in an Infant Following Excessive Intrauterine Irradiation.** F. W. Gunz, R. A. Borthwick, and G. L. Rolleston. Lancet 2: 190-192, July 26, 1958. (Christchurch Hospital, Christchurch, New Zealand)

The case of a 10-month-old infant who died from acute granulocytic leukemia is reported. The mother was very obese and, as there was doubt about the position of the fetus, three x-ray examinations were made during the last three weeks of pregnancy, with a total of five exposures, three of which were anteroposterior and two lateral. Because of the obesity, exposure factors were much greater than normal. It is estimated that the total dose to the center of the fetus was 25.35 r. Modifications of technic which have since been introduced would have diminished the dose received by the fetus by 92 per cent.

If irradiation caused the leukemia in the authors' patient, the latent period between irradiation and the onset of the leukemia was much shorter than that in Japan, which was upward of three years, or in the British series of irradiated spondylitics (two to five years). Since the patient was a very young infant, however, this short latency does not rule out a causal relationship. It may be significant that the leukemia was granulocytic, for nearly all post-irradiation leukemias have been of that type, either acute or chronic. An exception is the cases of lymphatic leukemia following irradiation of the thymus in childhood reported by Simpson *et al.* (Radiology 64: 840, 1955).

**Where Are the Cases of Radium Poisoning? A Plea for Assistance.** Samuel D. Clark. J.A.M.A. 168: 761-762, Oct. 11, 1958. (77 Massachusetts Ave., Cambridge 39, Mass.)

The author asks any doctor who has knowledge or clue as to the whereabouts of any person, living or dead, who falls in the following categories to notify the Radioactivity Center, Massachusetts Institute of Technology, Cambridge 39, Mass., immediately: (1) persons who ingested radium compounds of any sort, either therapeutically or in the course of their occupation, e.g., dial painting; (2) persons who received parenteral injections of radium compounds for such conditions as arthritis, hypertension, and gout; and (3) persons who suffered exposure in the process of radium research or the manufacture of radium products, as chemists, physicists, and laboratory assistants. As these cases are registered, the Radioactivity Center will work in close co-operation with the physician listing them, and all contacts with these persons will be made only through the reporting physician.

**Radium Poisoning: Two Case Reports.** G. M. Ardran and F. H. Kemp. Brit. J. Radiol. 31: 605-610, November 1958. (The Radcliffe Infirmary, Oxford, England)

Two cases of radium poisoning are reported.

The first patient was a 48-year-old male who gave a long history of multiple complaints. He was treated in 1936 with German "Radium Salt" injections. Two years later he was admitted to the hospital with severe anemia, weakness, and exertional dyspnea. Sternal puncture revealed marked bone marrow suppression. Body tissues showed excessive radioactivity. The patient died two months after admission.

The second case was that of a male radium technician, aged 53, admitted in February 1948 with anemia, thought to be due to radium exposure. There was a two-year history of increasing weakness. He had been seen for lumbago a year previously and had been found then to be very anemic. About this time there began to exhibit a deformity of the sternum and marked kyphosis. A "sarcoma-like" tumor was removed from the right little finger. Radiographic changes in the skeleton were interpreted as "those of myelomatosis." The patient died in March 1948.

Review of the literature shows the principal features of acute and subacute radium poisoning to be severe aplastic anemia, leukopenia, and necrosis of bone. Approximately 0.1 to 10 per cent of ingested or injected radium is eliminated; the remainder is practically all deposited in bone, the highest concentration being in the ends of long bones, the skull, and vertebrae. The resulting bone changes include irregular areas of diminished or increased density and areas resembling aseptic necrosis with sequestration. The authors suggest that all of these changes are due to death of bone, probably related to interference with blood supply.

Four roentgenograms; 1 photograph.

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**The Treatment and Care of the Irradiated Skin.** Karl-Heinz Kärcher. Strahlentherapie 107: 453-461, November 1958. (In German) (Czerny-Krankenhaus für Strahlenbehandlung der Universität Heidelberg, Germany)

Treatment and care of the irradiated skin will always

remain an important field for the radiation therapist, in spite of modern gamma-ray sources. The skin should be cared for during and after irradiation and in the presence of late sequelae. Compression of the skin to increase its tolerance should always be employed.

Daily use of ordinary talcum powder is recommended for the management of a mild reaction while the patient is under treatment. This has a cooling effect and keeps the skin dry.

Exudative reactions are treated with 2 per cent boric acid or 1:100 tannic acid dressings. If infection is present, 2 per cent Pyoktanin Violet or Castellani solutions combined with 1:1,000 to 5,000 potassium permanganate are added. After the infection has cleared up, ointments are used. It is essential to avoid a fatty base. Best results were obtained with 5 to 10 per cent dextrose and 1 per cent Paraxin in a water-soluble base. For thickened scars, hydrocortisone ointments have been of great value.

Late changes are managed identically. For infection, necrolytic ferments are recommended. Large necrotic areas have to be treated surgically.

Eight photographs; 1 diagram.

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**Automatic Dodging of X-ray Exposures to Reduce the Dose and Increase the Information.** Bertil Jacobson. *Lancet* 2: 1101-1102, Nov. 22, 1958. (Karolinska Institutet, Stockholm, Sweden)

Many improvements can be made in order to reduce the dose during diagnostic x-ray procedures and to increase the information obtained at each exposure. There are optimum wavelenghts for obtaining the maximum amount of contrast per dose given and, similarly, there is an optimum exposure time. A system for setting the exposures is described. The x-ray focus, the patient, and the film are all fixed in position. A slit-shaped window, allowing only a flat, narrow beam of x-rays to pass the object, is placed in front of the tube. At each exposure the slit moves so that the beam scans the patient once. A number of tiny shutters are placed in front of the slit. At each instant during the scanning, these shutters allow the exact amount of radiation to pass for optimal exposure of the corresponding film area. The shutters are controlled by an electronic feedback system from a number of ionization chambers (or scintillator photomultiplier units) which sense the amount of radiation leaving the patient. Each shutter has a corresponding sensing unit, though there is some overlap. The sensing units are placed behind the screen-film combination, since sufficient quanta penetrate it. Each shutter controls an area of about 1 sq. cm. of the image at each instant of the scanning. No images of the shutters appear on the film, since they are placed close to the tube focus.

Experiments with a simple one-channel system have proved that the system works. Two-dimensional scanning was used, although it would be necessary in practice to employ a one-dimensional scan with several parallel channels of x-ray beams. The load on the tube will increase by a factor equal to the ratio of the width of the film to the width of the x-ray beam projected onto the film (the lengths of the film and the beam are equal). This might necessitate the construction of new types of tubes. The choice of tubes must be considered also in order to determine the optimum wavelength for reducing the dose. Tubes capable of carrying larger

currents than the present ones would be required in both cases.

One drawing.

**Ultraviolet Microscopy of X-Irradiated Intestine.** Yvette S. Lewis, Henry Quastler, and George Svihla. *J. Nat. Cancer Inst.* 21: 813-823, November 1958. (Argonne National Laboratory, Lemont, Ill.)

The salient feature of the investigation described here was the use of the color-translating ultraviolet microscope in the study of radiation effects in the intestine. The animals employed were 31 young adult female CF #1 mice kept under standard laboratory conditions. Five mice were retained as controls and most of the remainder were given 2,000 r or 600 r of whole-body irradiation. The radiation factors were 250 kvp, filter 0.5 mm. Cu plus 3 mm. Bakelite (h.v.l. 1.5 mm. Cu), dosage 245 to 260 r per minute. The two dosage levels were selected because 2,000 r can be counted on to block cell production long enough to cause denudation of the intestine and subsequent death, and 600 r is known to block production of cells for approximately eighteen hours, after which recovery ensues.

All descriptions are given in terms of absorption of 263  $m\mu$  ultraviolet. Generative cells showed pronounced changes in light absorption at 263  $m\mu$ ; the light-absorbing clumps normally present in the nucleus disappeared. Later, diffuse, strong absorption was seen in cytoplasm and nucleus; still later, there was very little absorption. The earlier changes occurred uniformly in all generative cells and thus cannot be related to a stage in the mitotic cycle; the late changes were independent of resumption of mitosis. The principal cells had similar but much less pronounced changes in 263  $m\mu$  absorption. Subsequently, changes took place that were related to abnormal development. The Paneth cells, which are highly radioresistant if survival is taken as a criterion, showed similar changes in 263  $m\mu$  absorption. In addition, early degeneration of a specific (secretory) cytoplasmic structure was revealed in these cells, followed by speedy recovery.

All these findings could have been made without the ultraviolet microscope. It is the authors' impression, however, that it is difficult to match the overall amount of information of various kinds that can be derived from watching the color-translated pictures. The instrument in its present form is difficult to handle and its performance is definitely short of perfect, but it is hoped that future improvements will make its advantages more readily accessible.

Ten photomicrographs.

**Species Differences in Response to High Radiation Doses.** Howard L. Andrews. *Radiation Res.* 9: 469-477, October 1958. (Radiation Branch, National Cancer Inst., Bethesda, Md.)

Survival times were studied in mice, rats, guinea-pigs, and hamsters at doses up to the point where irradiation times become an appreciable fraction of total survival time. The survival time data revealed rather surprising species differences, the most striking being the sharp transition in the guinea-pig and the mouse. Although both species showed intense central nervous system involvement at doses above the transition, there are definite differences between the two. All attempts, including the use of a variety of drugs and fractionated dose schedules, failed to close the gap

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between thirty hours and one hundred and ten hours in the guinea-pig. Mice, on the other hand, showed a graded survival time at the transition dose. Qualitatively the responses of the rat and hamster were quite similar.

Results of shielding experiments suggest that radiation received by the head has a negligible effect below the transition dose but is all-important above it.

The only high-dose whole-body exposures in man occurred in the Hiroshima and Nagasaki bombings. In most cases blast and secondary missile injuries obscured radiation effects. In 2 Hiroshima cases, burns may have had little effect on survival: in a fifteen-year-old boy, survival time was one hundred and twenty-two hours; in a thirty-two year-old man, it was one hundred and forty-eight hours. The combined radiation dose in these cases is estimated as 9,000 rem. At this dose man does not appear to be far different from the rodents studied.

Five graphs; 1 table.

#### **Radiation Injury and Marrow Replacement: Factors Affecting Survival of the Host and the Homograft.**

Joseph W. Ferrebee and E. Donnell Thomas. *Ann. Int. Med.* 49: 987-1003, November 1958. (Mary Imogene Bassett Hospital, Cooperstown, N. Y.)

The authors review the experiences of others who have employed total-body irradiation of 500 to 1,000 r in animals. Doses in this range are usually followed by death in seven to fourteen days, due to failure of marrow function. In a number of animal species death from this cause can be avoided by an intravenous infusion of homologous marrow cells twenty-four to forty-eight hours after exposure.

Some patients with leukemia have been given 200 to 600 r of total-body irradiation and an infusion of normal marrow from suitable cadavers or volunteers. In some cases worthwhile remissions have occurred. In others, the benefit has been only temporary. It seemed to the authors advisable to record the guiding principles that have emerged from these preliminary studies in man and relate these principles to the abundance of information now becoming available from experimentation in other species.

In the field of homograft immunology, two basic biologic phenomena have been recognized which are useful: (1) Billingham's actively acquired tolerance, and (2) the discovery of radiation chimeras. These latter are, in some respects, the counterpart of the transmutation of elements and our chief biologic inheritance from a troublesome atomic era. A radiation chimera, by definition, is an animal whose defense mechanism has been rendered inoperative by total-body radiation and which, because of marrow damage and a paralyzed immune mechanism, accepts marrow homografts without reaction. These marrow grafts are, because of their reparative action on the damaged bone marrow and immune mechanism, often lifesaving.

A mature individual is tolerant of himself; that is, he has something in his defense mechanism which enables him to use marrow grafts from himself but causes him to reject those of others. There is a time in fetal or early neonatal life when this discriminatory power is absent, at least in many species. It is absent even in dizygotic twin calves by virtue of the vascular anastomosis between the placentas. Twin calves share primitive marrow cells, blood groups, and accept homografts of skin or kidney.

In the rodent the pattern of self recognition in the immunological defense system is not rigidly set during the first neonatal day, and injection of a few marrow cells from a prospective donor at that time readily establishes tolerance. Rodents thus prepared will exchange tissues in later life but only with the donor to whom they were earlier conditioned. Tolerance acquired to essential cell antigens during a ductile state in early or neonatal life is, like immunity, a relatively permanent acquisition.

Radiation doses of such magnitude as to stop antibody formation and paralyze the defense mechanism make possible homograft transplantation. This is often a life-saving measure, as it brings about reconstitution of the bone marrow, partial restoration of the lymphoid elements of the blood, and incomplete repair of the immunologic defense mechanism. An animal so irradiated and then given a bone marrow infusion is an example of a radiation chimera. The altered defense mechanism is that of the donor, not that of the recipient. The subjects so treated remain immunologic cripples.

A consideration of the above biologic phenomena led the present authors and others to give high doses of total-body irradiation and marrow-toxic drugs to man, followed with homograft marrow infusions. The patients most commonly treated were suffering from blood dyscrasias. One patient with uremia was thus irradiated and given bone marrow, and had a kidney transplanted. The materials injected were fetal hematopoietic tissues and frozen and fresh cells from cadavers. These injections have been done many times without the development of signs or symptoms. The manner of preparation and injection of the materials is described in considerable detail.

One patient with leukemia was given a mean tissue dose of 300 r of total-body irradiation with a 250-kv therapy machine and an infusion of bone marrow from her sister. By use of antibiotics she was carried through a two-week period of recurrent fever and infection. She had a very satisfactory response but probably will have a recurrence.

Many questions remain unanswered. Among them are: (1) What is the optimum dose? (2) At what rate should it be given? (3) What are the proper radiologic facilities for total-body irradiation in man? The usual radiologic equipment is inadequate for this type of radiation treatment. The restoration of the lymphoid defense mechanism and management of infection are a difficult subject and require further exploration.

Infusion of marrow cells after lethal total-body irradiation is a simple method of avoiding acute death from lethal radiation exposure in the 1000-r range in some species. We should endeavor to learn as much about it in man as possible, as soon as possible, for reasons that are self evident.

This is a valuable and interesting article. Eight explanatory figures are included.

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#### **Preliminary Observations on the Treatment of Post-irradiation Hematopoietic Depression in Man by the Infusion of Stored Autogenous Bone Marrow.**

N. B. Kurnick, Andrew Montano, James C. Gerdes, and Bernard H. Feder. *Ann. Int. Med.* 49: 973-986, November 1958. (VA Hospital, Long Beach 4, Calif.)

The authors summarize the experimental knowledge

of radiation effects upon the hemopoietic tissues and the achievement of protection against lethal irradiation as accomplished in animals by infusion of homologous bone marrow.

Radiation-protective bone marrow can be preserved for as long as eighty-three days stored under certain specific conditions. The preserved bone-marrow cells can repopulate the depleted bone marrow of the recipient. Thomas *et al.* (New England J. Med. **257**: 491, 1957. Abst. in Radiology **71**: 153, 1958) were able to demonstrate in one patient the presence of circulating erythrocytes of the donor type three weeks after infusion.

Possible reasons for the failure of bone marrow to result in prolonged "takes" are discussed. After a consideration of the difficulties encountered with homologous grafts, it occurred to the authors that these complications could be avoided by using autogenous bone marrow grafts. The clinical application of the idea seemed reasonable.

Autogenous bone marrow grafts were used in 2 reported cases: a teratocarcinoma of the testicle and a renal carcinoma with pulmonary metastasis. Prior to irradiation of these 2 patients, bone marrow was collected and preserved by the Polge technic (see Barnes and Loutit: J. Nat. Cancer Inst. **15**: 901, 1955. Abst. in Radiology **66**: 161, 1956). The marrow was given at appropriate intervals following irradiation of the patients. Serial bone marrow examinations demonstrated severe hypoplastic marrow at the completion of radiotherapy and showed that repopulation of the bone can occur within a two- to four-week interval. Other patients who suffered a less severe degree of bone marrow depression than the 2 cited here required two to nine months for recovery from marrow hypoplasia without the use of infusions.

No reactions of immunologic nature such as occur with homologous grafts were encountered. It can be said with certainty that these autogenous grafts were innocuous and may well have been responsible for the relatively rapid recovery from bone-marrow hypoplasia produced by irradiation. This method may be useful in potentially curable cancer requiring wide and rapid irradiation. Such patients are often denied adequate irradiation treatment because of the danger of producing fatal bone-marrow depletion. This method seems most worthy of further clinical trial where indicated.

Ten photomicrographs; 4 graphs.

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**Relative Biological Effectiveness of Various Qualities of Radiation as Determined by the Electroretinogram.** Norman A. Baily and Werner K. Noell. Radiation Res. **9**: 459-468, October 1958. (Roswell Park Memorial Inst., Buffalo, N. Y.)

A knowledge of the relative biological effectiveness (RBE) of various qualities of x-radiation is important for the evaluation of the effects produced and perhaps to furnish information on the nature of the mechanism of biological damage due to the action of ionizing radiations on living tissues. The biological system used in the present investigation was the rabbit retina. Here, the visual cells show a differential sensitivity to ionizing radiation; they are destroyed by amounts of radiation well below that necessary to produce death of the other cell populations of the retina.

A tool for the quantitative evaluation of x-ray damage

to the visual cell is provided by the electric potential recorded as the "electroretinogram" (ERG) from the cornea or the anterior chamber. The magnitude and characteristics of this response to light stimulation are dependent on the functional state of the visual cell. Exposure of these cells to x-radiation may abolish this response. When the absorbed dose is above a certain minimum value, the response is decreased or eliminated suddenly and irreversibly. The time lag between the observed effect and the attainment of the minimum absorbed dose is usually less than four minutes. The absorbed dose at which these effects manifest themselves shows only small variations from animal to animal. It is this factor that permitted the use of the ERG as a quantitative measure of the RBE. The dose levels that produce these acute effects on the ERG also result in cell death within twenty-four hours, making possible histologic confirmation of the electrical measurements.

The acute and irreversible effects on the electroretinogram were used to determine the RBE of 100-kvp, 250-kvp, and 2,000-kvp x-rays on the rabbit's visual cells. The results obtained by this method were similar to those obtained by histological determination of cell death.

In this system, the relative biological efficiency was found to increase with decreasing linear energy transfer. The average values determined were  $0.722 \pm 0.011$  for 100-kvp x-rays,  $1.00$  for 250-kvp x-rays, and  $1.30 \pm 0.02$ , and  $1.31 \pm 0.08$  for x-rays generated at 2,000 kvp when the radiation was delivered to the eye anteriorly, posteriorly and posteriorly-anteriorly, respectively.

Four figures; 4 tables.

**Immediate Effects of Irradiation of Elastic Tissues with X Rays, Radium, and Radioactive Cobalt.** Stefan Jellinek. Lancet **2**: 1149-1151, Nov. 29, 1958. (University of Vienna, Vienna, Austria)

The immediate effect of irradiation on elastic tissue was investigated in the ligamentum nuchae of calf fetuses and the skin of 5 recently deceased human beings. X-rays, radium, and radioactive cobalt were used for doses ranging from 1 r to 50,000 r. At first sight the wide range of dosage as a cause of comparable histologic effects seems surprising, but according to the author there is a corollary in the range of 4 r to 70,000 r of the sublethal effects on cell mitosis (Spear: Brit. J. Radiol. **31**: 114, 1958). The effects observed were all broadly alike, whatever the method of irradiation employed. If anything, an equivalent radium dosage seemed to have the greater effect on elastic tissues. Basically, the changes were of two types: (1) morphologic changes consisting chiefly in fragmentation and disarray of the fibers, suggesting a mechanical mode of action of the irradiation, and (2) changes of inner texture, suggesting physicochemical mechanisms and demonstrated by swelling of the elastic fibers, their impaired staining capacity and partial transparency, and the enigmatic debris formation between fibers.

Eight photomicrographs.

**Radiation Dose Measurements and Leucocyte Count in Rabbits.** M. Helde, T. Wahlberg, A. Forsberg, B. Swedin, C.-J. Clemensson and A. Nelson. Acta radiol. **50**: 477-489, November 1958. (Institute of Radiobiology, Karolinska Institutet, Stockholm)

A controlled study of the changes in the leucocyte count in male rabbits as a function of irradiation is re-



ported. Blood values were plotted and interpreted by the "read-off method," which is described. The frequency of changes was found to be primarily related to the dose-rate rather than to the total dose administered. The dose-rate in this instance is defined as mr per (very short) unit time of irradiation. This very short unit time is designated "the biological relevant time."

The authors state that their observations in rabbits seem to verify previous observations in human subjects. In both instances the best correlation between irradiation data and biologic effect was obtained when the irradiation data were calculated in dose quantity per "very short" time.

Five diagrams; 4 tables.

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#### Time-Dose Relationship and Morphology of Delayed Radiation Lesions of the Brain in Rabbits. Nils O. Berg and Martin Lindgren. Acta radiol. Suppl. 167, 1958. (University Hospital, Lund, Sweden)

A considerable body of evidence has now accumulated regarding the sensitivity of brain tissue to radiation, but most of this concerns the effect of a single dose of radiation given in a relatively short time. There is little or no experimental evidence regarding the time-dose relationship in the reaction of the central nervous system to radiation. The authors set out with four objectives: to determine the time-dose relationship for delayed reactions of the brain tissue of rabbits, comparing single dose and fractionated dose; to simultaneously determine time-dose relationship for skin tolerance; to chart the extent and character of the lesions produced in the central nervous system; finally, to correlate the clinically visible changes with the localization of the cerebral lesion.

Rabbits were used as test material, since they are easily handled and readily available in large series. Irradiation was given to half of the head, without anesthesia. The radiation source was operated at 200 kv, with a half-value layer of 0.93 mm. of Cu. Exposures were given at a focal skin distance of 25 cm., at which distance the dose rate was 105 r per minute in air. On the basis of published data, dose distributions in the heads of the animals were calculated. Three schedules of treatment were used—single dose irradiation, daily treatment for twelve days, and daily treatment for thirty days. Several dosage levels were investigated, at each of these fractionations. Nearly all animals were sacrificed and studied at fifty-two weeks; only a small proportion did not survive for that length of time.

The effects of the radiation on the skin were analyzed from the standpoint of epilation, atrophy, and necrosis. The doses required for a 50 per cent incidence of epilation and necrosis gave parallel lines when plotted on double logarithmic paper. The slope of these lines was about 0.33. It is noted that this differs from the slope found by Strandqvist for human skin, which is 0.22.

The pathologic changes found in the brains of the irradiated animals are discussed in detail. In general, gross change was not striking, occasional animals showing areas of massive destruction, a few exhibiting cysts and abscesses. Microscopically, three types of change were noted. Many of the animals showed fine discrete changes in otherwise undamaged brain. These included small petechial hemorrhages, vessel changes in the brain or in the meninges, and small glial scars. The second group consisted of instances of partial destruc-

tion, including myelin destruction in the white matter, lesions in the gray matter with single intact nerve cells, and fibrinoid staining of the tissue, without necrosis. A third group consisted of recent and old necrotic changes, cysts, and complete glio-vascular destruction.

The authors were unable to correlate the symptoms shown by the animals with the localization of brain damage. The general reaction varied from stormy acute symptoms to gradual deterioration with the appearance of one or more neurological signs. In general, the more acute reactions were associated with single dose irradiation. Many animals had symptoms of a vestibular type, such as wry neck, disturbances of balance, nystagmus, etc., which were not accounted for by changes in the brain substance. More extensive examination of extracerebral structures showed lesions in the labyrinth in a high proportion of these animals, some on the basis of purulent otitis, others apparently the result of radiation effect *per se*.

On the basis of the pathologic findings, the data from the three dose plans were examined in terms of doses of different fractionation producing equivalent effects. The data, when plotted, resulted in curves with slopes varying from 0.29 to 0.43. The mean slope was 0.34, which the authors consider represents a good average value for the rabbit's brain with the type of irradiation used.

In this study the authors found a slope of 0.33 to 0.34 for the fractionation curves for rabbit skin and rabbit brain. This appears to be significantly different from the slope of 0.27 derived by Du Sault (Am. J. Roentgenol. 75: 597, 1956. Abst. in Radiology 68: 148, 1957) for skin tolerance in man. The authors state that, on the basis of their experimental investigation, "it appears justified to assume that in other mammals, including man, the slope of the time-dose relationship curve for the brain will be the same as for the skin."

A comparison of the effect of certain dose levels in this study in general correlates quite well with that presented in previous studies. There seems to be greater sensitivity of the white matter to radiation than of the gray matter, as has been previously noted.

The morphologic character of the lesions found would tend to support the concept that vascular damage is the initial stage in radiation damage to the brain. The discrete lesions described are of varying size and would appear to be scars representing healing stages of a radiation reaction which is not necessarily progressive. There was no evidence to support the concept that uncomplicated delayed radionecrosis represents the end-result of inflammatory reaction of lymphocellular type. The predilection of radiation damage for the white matter rather than the gray could be explained on differences in the vascular pattern of the two areas. The vascular network is much more abundant in the gray matter, and thus, damage to a particular vessel in the white matter would tend to produce a larger more severe lesion. The authors call attention to the fact that a number of cerebral diseases of uncertain pathogenesis show a particular predilection for the white matter, such as multiple sclerosis, acute disseminated encephalomyelitis, etc. The early lesions in all of these diseases exhibit a more or less definite relationship to the vessels in the white matter.

Seventy-two figures; 19 tables.

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**A Comparison of the Effects of Radioactive Internal Emitters and X-Rays on Antibody Formation.** Paul R. Salerno and Hymer L. Friedell. *Radiation Res.* 9: 478-486, October 1958. (H. L. F., Western Reserve University School of Medicine, Cleveland, Ohio)

The relative effectiveness of radiation injury produced by radioactive colloidal gold ( $\text{Au}^{198}$ ) and  $\text{P}^{32}$  was compared with that of x-rays on the *primary* antibody response to a single injection of *particulate* antigen in the form of washed sheep erythrocytes. Findings were as follows:

A threshold dose of 390 r of total-body x-rays suppressed the capacity of the rat to synthesize antibody in reaction to antigen injected two to twenty days post-irradiation.

Large doses of  $\text{P}^{32}$  did not significantly reduce the ability of the rat to synthesize antibody to sheep erythrocytes.

Colloidal  $\text{Au}^{198}$  injected six days before treatment with antigen elicited a partial suppression of antibody formation.

Combinations of  $\text{P}^{32}$  with x-rays or with  $\text{Au}^{198}$  did not enhance the depressant action on antibody synthesis.

Combined treatment with suboptimal doses of x-rays and  $\text{Au}^{198}$  greatly increased but did not completely suppress antibody production.

These results indicate that ionizing radiation must be delivered to the total body to produce quantitative inhibition of antibody synthesis. The significant but incomplete suppression produced by  $\text{Au}^{198}$  suggests that integrity of the reticuloendothelial system is required for maximal antibody production. The ineffectiveness of  $\text{P}^{32}$  alone or in combination with  $\text{Au}^{198}$  indicates that the bone marrow is not a major site of antibody formation. The enhanced initial rate of antibody synthesis in animals sustaining selective radiation injury to the bone marrow is most likely due to an increase in activity of the spleen. Many tissues escape severe radiation injury by both  $\text{Au}^{198}$  and  $\text{P}^{32}$ , and some of these may be important in antibody formation, *e.g.*, the thymus and smaller lymph nodes of generalized body distribution. Adrenalectomy did not detectably alter the effect of 390 r in suppressing antibody formation. This last finding is in keeping with the premise that the effect of x-rays is direct on many separate

tissue systems. It is also in keeping with a specific cellular mechanism in the antigen stimulation of antibody formation.

Six graphs.

**Immunogenetic Studies on X-Irradiated Mice Treated with Homologous Hematopoietic Cells.** Michael Feldman and David Yaffe. *J. Nat. Cancer Inst.* 21: 697-712, October 1958. (Weizmann Institute of Science, Rehovoth, Israel)

An analysis was made of the immune reactions taking place in x-irradiated mice treated with homologous hematopoietic cells. The results of experiments with hybrid combinations of hosts and donors suggest that the grafted cells react immunologically against the isoantigens of the irradiated recipient. The production of anti-C3H agglutinins by the inoculated C57BL cells was demonstrated by the transfer of lymph nodes from the irradiated and treated C3H mice back to normal C57BL mice. The "cyclolethal" anti-host immune reaction responsible for the lethal "secondary disease" of homologously treated mice was demonstrated by the passive transfer of transplantation immunity produced by the isoantigens of the recipient. Bone marrow from irradiated C3H mice treated with C57BL cells conferred on other irradiated C3H mice a much shorter survival time than normal C57BL cells.

It is concluded that the cells from the C57BL-treated C3H donors were immunologically activated by the primary C3H hosts and killed the secondary C3H hosts through an immunologically secondary response. The mortality of mice treated with mixed embryonic isologous and adult homologous cells indicates that even if, theoretically, a delayed anti-graft response is feasible, the graft antihost response has a dominant role in the immunogenetic incompatibility. An attempt to overcome this incompatibility was made by injecting irradiated C3H mice with fetal C57BL liver cells.

The increased survival time obtained in this experiment may suggest a method for the application of the principles of biological protection to animals of genetically heterogeneous populations.

Eight tables.

AUTHORS' SUMMARY



1980

specific  
anti-

Mice  
fibro-  
blast  
trans-

transformations  
inhibitors  
agents  
against  
The  
effect of  
C3H  
"toxic"  
ethanol  
in mice  
trans-  
formation  
of  
C3H  
cells  
in  
culture

TBL-  
transformed  
primary  
diploid  
cells  
anti-  
trans-  
formation  
com-  
patibility

peri-  
pheral  
necro-

cyte